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FUNCTIONING TUMOURS OF THE OVARY, WITH SPECIAL REFERENCE TO PATHOLOGY AND HISTOGENESIS*

BY

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MY first pleasant obligation, and certainly not a merely conventional one, is to express my great appreciation of the honour of being invited to deliver this address before your distinguished College. I am proud to be the first of my countrymen to fill this new lectureship, which the generosity of one of your Fellows has made possible and which should do much to bind even more closely the followers of our specialty in our two countries. I am also deeply grateful to you for bestowing upon me the Honorary Fellowship of the Royal College, an honour which I can assure you I shall always cherish. It is not false modesty on my part to feel that this distinction is intended as a friendly tribute to American gynaecology and obstetrics, no less than to any very modest contributions of my own in our common field of endeavour. Many of your own distinguished leaders have appeared before the national societies of our country, and the names of not a few are inscribed among our honorary fellows.

The choice of my title is easily explained by the fact that, while my interests have always been primarily clinical, my scientific hobbies, if one may use such a term for interests which are such important, and such integral, parts of one's daily clinical work, have been in the fields of pathology and endocrinology.

The tumours which I propose to discuss to-day are of great clinical importance in spite of their comparative rarity, but their pathologic characteristics are of rather special nature, and not as widely recognized as are those of many other neoplastic types. The fact that these tumours have the capacity of producing striking sex changes, because of their hormone-producing capacities, surrounds them with a sort of scientific glamour not possessed by other ovarian tumours.

A final consideration in the selection of my title lies in the fact that I have had the

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opportunity of studying material from an unusually large number of tumours of the type I am to discuss. Only a small fraction of this material comes from our own clinic. For that matter no one clinic in the whole world can boast of a very imposing number of these comparatively uncommon tumours. However, a large number of cases have been made available to me through the fact that material has been sent in for diagnosis from many other clinics in our own country, as well as others. During the past four years, moreover, the Ovarian Tumor Registry, sponsored by the American Gynecological Society, has brought to us an ever-increasing amount of ovarian tumour material, including a surprisingly large number of functional ovarian tumours. This material is stored in our own laboratory, since I have served as the Chairman of the Ovarian Tumor Committee since its inception. The Registry material will ultimately give us a rich storehouse of well-authenticated material, with complete clinical data, and a reasonably good follow-up. The large number of cases studied before the inauguration of the Registry are of more value for pathological than for clinical studies, since so many of them come from small hospitals from which it is extremely difficult to obtain satisfactory histories, much less follow-up reports.

No longer is the concept of functioning tumours of the endocrine glands a new one, and a considerable group of such tumours is now well recognized as producing characteristic clinical syndromes. The gigantism or acromegaly associated with eosinophilic adenoma of the anterior pituitary, the Cushing syndrome produced either by basophilic adenoma of the pituitary or adenoma of the adrenal cortex, the profound sex changes produced by certain tumours of the adrenal, and the characteristic syndromes associated with tumours of the parathyroid and the pancreatic islands of Langerhans are among the better known examples of the biological effects of endocrine gland tumours.

In so far as the ovary is concerned, it has been established that hyperthyroidism may result from over-activity of the thyroid tissue contained in the ovarian teratomatous tumour known as struma ovarii. In the most recent report on this subject, Emge (1940) collected a good many instances of this sort, including the one observed by himself. With this group of functioning tumours arising from tissues alien to the ovary I shall not deal in the present paper, which will be devoted to certain functioning tumours made up of tissues intrinsic to the ovary itself.

It was Robert Meyer (1933) who, through a study of his own material, and a critical analysis of that included under various designations in the publications of previous authors, gave us a grouping of these "special" ovarian tumours, as he called them, which is still acceptable to-day. Moreover, he gave us what, on the whole, has proved to be a satisfactory working theory as to the histogenesis of tumours of this group. The importance of his contribution is not lessened by the fact that his original views on this point have, in spite of the canonical weight carried by his pathological prestige, seemed to require modification or supplementation on various points, as will be discussed later.

While my paper will include a brief discussion of some of these moot points as to histogenesis, it will concern itself even more with the characteristics of the tumours from the fairly well-established standpoint of their pathology. The clinical effects of these tumours are now quite well known, and will be included in this discussion simply for the purposes of correlation.

There are three ovarian tumour-types which are derived from cells dating back to

the very early phases of gonadal development. Two of these are of functioning nature, and one is endocrinologically inert, but it is difficult to exclude its brief discussion as a sort of background in the consideration of the other two varieties. Any intelligent concept of the nature and biological potentialities of these tumours presupposes at least some knowledge of early ovarian embryology, although even on this point our knowledge is still far from complete.

Endocrinologists, however, are agreed that, in its earliest phases, the ovarian anlage cannot be histologically differentiated from that of the testis. In this undifferentiated phase, certain cells may become segregated from the later differentiating processes going on in the gonadal area, remaining dormant and undifferentiated until postnatal life, when they may give rise to the tumour type to which Meyer gave the designation of dysgerminoma.

If the above explanation is correct, one would expect the resulting tumour to be lacking in endocrine effect, since the constituent cells date back to a phase in gonadal development when neither ovarian nor testicular characteristics had appeared. This is in conformity with clinical experience, as no case of dysgerminoma has been reported as producing endocrine effects. Some of the earlier observations on such tumours appeared to suggest such an influence. Quite a number were described as occurring in definitely intersexual individuals, including pseudohermaphrodites. However, after the removal of such tumours the individuals remain just as intersexual as ever. In other words the tumours have nothing to do with the production of the intersexuality, which is of the common congenital or genotypic variety.

Again, if the above-mentioned concept is correct, one would expect to find dysgerminomas in the testis as well as in the ovary, and this is actually the case. The relatively common seminoma of the male gonad is histologically identical with the ovarian dysgerminoma. Indeed, in the French literature the latter is still quite generally spoken of as seminoma (Chevassu).

In a now considerable group of reported cases dysgerminoma has been found in association with unquestioned teratomatous elements, and I have seen a small group of such cases. This fact has led some to the view that dysgerminoma itself is to be explained as a teratoma, in spite of the fact that the overwhelming proportion of these tumours are histologically completely lacking in any of the usual teratomatous admixtures. For the present it would seem that we are justified in adhering to Meyer's original explanation of the origin of these tumours, since it conforms so completely with what we know as to their clinical characteristics.

The characteristic microscopic pattern is that of rather large, round or polyhedral cells arranged in alveoli, separated by septa of usually hyalinized connective tissue showing lymphatic infiltration (Fig. 1).

Since dysgerminoma is not a member of the functional group it does not seem necessary to dwell upon its clinical or pathological characteristics except in very cursory fashion. Such tumours occur characteristically in young patients (carcinoma puellarum), usually in the teens or twenties, sometimes later, but only rarely over 50. They are usually of small or moderate size, but may become very large, filling most of the abdomen, as in the very first case we encountered in our own laboratory, in which the patient was 7 years old.

They are primarily solid, but as they grow their necrotic tendency may produce small or large ragged cavities. The smaller tumours are well encapsulated and of

moderately firm or doughy consistency. As they grow, however, the capsule is apt to be penetrated, the tumour becoming widely infiltrative, this greatly increasing its clinically malignant potentialities. As a matter of fact, if there is any criterion for the selection of radical over conservative operation in the young individuals in whom such tumours characteristically occur, it would probably be this factor of large size and, even more important, local infiltration through penetration of the capsule.

The smaller well-encapsulated growths may be treated conservatively, with unilateral adnexal removal, and of course without postoperative irradiation in the young individuals of this group, often girls in their teens. However, it must not be assumed that cure invariably occurs in this favourable group, while recurrence is common in the infiltrative variety above described. We have recently observed a well-encapsulated dysgerminoma of the size of an orange, in which a radical operation was done, including hysterectomy and bilateral salpingo-oöphorectomy, although the patient was only 28 years old. Within 3 months the patient died of mediastinal metastasis, the autopsy showing no local recurrence in the pelvis.

In our own laboratory material we have studied 43 cases of dysgerminoma, although only a fraction of these were observed clinically in our hospital. A follow-up has been possible in only a fraction of our cases, and thus far the overall recurrence-rate of dysgerminoma would seem to be in the vicinity of 20 to 25 per cent, the figure arrived at by Novak and Gray (1938) in an earlier study of 17 cases from our laboratory.

Masculinizing Tumours.

The early undifferentiated or neutral phase of gonadal development is followed after 5 or 6 weeks by one in which the gonadal area shows evidence of differentiation, with the appearance of anastomosing sex cords made up of cells differentiated *in situ* from the gonadal mesenchyme. This statement is made rather arbitrarily, since it is now supported by convincing evidence, and is accepted by practically all embryologists. The former viewpoint, that the sex cords are produced by invagination of the surface epithelium, appears to have been largely abandoned, although there is still some doubt about the possible role played by certain accessory or secondary sex cords which have been described by Gruenwald (1942).

In the gonad destined to become a testis, the sex cords later, through canalization, become the seminiferous tubules, linking up with the mesonephric structures to form the complete testicular apparatus (tubules, vasa recta, rete and vas deferens, the latter being, of course, derived from the Wolffian or mesonephric duct). As we are more directly concerned with the ovary, it is important to emphasize that exactly the same testicular scaffolding is first laid down, that in the ovary this is evanescent, that it is succeeded by a second wave of more typically ovarian differentiation, but that vestiges of the original testicular structure may persist in the later life of the ovary. This is an over-simplification of these early embryonic changes, concerning some of which there is still some uncertainty, and which probably progress in more or less overlapping fashion. However, it conforms to accepted general principles, and is of service in the explanation and interpretation of the group of tumours under discussion.

The statement made above to the effect that the medulla of the ovary contains vestiges, at times demonstrable even histologically, of cells which started off along testicular lines, justifies the frequent state-

ment that there is a potential testis in every ovary. It is from these potentially testicular cells, according to the concept of Meyer, that neoplasms may arise which, as might be expected, reproduce testicular histology to some degree or other, and which, through the production of the testicular hormone, exert a masculinizing effect upon the female organism.

Attractive and rational though this theory may be, it is only a theory, and it cannot be accepted without question. It has always seemed to me that we cannot close our eyes to the very intimate relation, in the early phases of embryonic life, of the ovarian medulla and the adrenal cortex. These virtually blend one with the other, and it is therefore not surprising that the effects of arrhenoblastomas and of certain adrenal cortical tumours are quite similar. This still does not explain the origin of arrhenoblastoma satisfactorily, although it would be highly suggestive as regards the histogenesis of the so-called adrenal rest tumours of the ovary. The arrhenoblastomas, on the other hand, tend to reproduce testicular structure, so that an origin from testicular or pro-testicular structures would seem more likely.

Nor are these the only hypotheses which have been advanced on this point. As already stated, embryologists now believe that the gonadal mesenchyme is embryologically the mother tissue from which both testicular and ovarian elements are derived, and this would apply not only to such parenchymal structures as seminiferous tubules and ovarian follicles, but also to the interstitial or stromal elements of both testis and ovary. The stroma might therefore be expected to retain a great deal of differentiating potency, in fact a totipotency in so far as differentiation into either masculine or feminine elements is concerned. An increasing number of authors, therefore, have stressed this latent mesenchymal differentiating potency as explaining the testicular character of certain ovarian tumours.

This theory is not very different from that of Meyer in so far as arrhenoblastoma is concerned, but it can be extended, and has by some been extended, to explain the masculinizing group of tumours variously described as adrenal tumours of the ovary, masculinizing luteoma, masculinovoblastoma or virilizing lipoid cell tumours. Teilum (1944, 1946) believes that tumours of this group are really to be interpreted as interstitial or Leydig cell tumours, their characteristic adrenal-like cell constituents arising from the ovarian mesenchyme, which can give origin to any element of testicular structure. There can as yet be no general application of this concept, the evidence still indicating that most tumours of this group are really of adrenal type. In spite of the fact that at least a few masculinizing luteomas have been reported, I agree with Schiller (1933) that these are actually to be interpreted as adrenal in character. Since adrenal rests are rarely seen in the adult ovary itself the occurrence of such tumours would seem most logically explainable by embryological segregation or adrenal cells in the gonadal area, as a result of the embryological intimacy and continuity of the adrenal cortical and ovarian medullary areas in early development.

Another view, urged by Iverson (1947), is that the so-called adrenal tumours are really made up of luteinized theca interna cells. From the standpoint of mere morphology, there is no doubt that these theca cells can assume an appearance quite like that of the cells of the adrenal zona fasciculata, and it is difficult to avoid the feeling that they must have an important function, though no one knows what it is. It was these very theca cells, luteinized and hypertrophied in late stages of pregnancy,

which were at one time spoken of as the interstitial cells of the ovary (interstitial-druse) analogous to the interstitial or Leydig cells of the testis, a view for which no scientific support has ever been adduced.

Even in the non-pregnant woman one is often struck by the marked hypertrophy of this thecal layer surrounding atretic follicles, the cells becoming large and polygonal, with often an alveolar arrangement which increases their resemblance to adrenal cells. Culiner (1945) has even suggested that changes in these thecal cells may be responsible for menstrual disorders, but the evidence he furnishes is not convincing. I have recently examined sections of the ovaries from two infants, one 3 months old and the other 16 months old, in which this thecal change surrounding atretic follicles was very striking, and very reminiscent of adrenal cells. It would seem that only certain phases of atresia folliculi show this thecal responsiveness (Fig. 2).

We know too little as to the significance of these thecal changes in atretic follicles to justify any prolonged discussion, and they are mentioned here simply to emphasize that the ovarian mesenchyme, which is a progenitor of theca as well as of the granulosa, probably possesses differentiating potentialities which have not been fully appreciated. It is, as a matter of fact, not impossible that the histogenesis of the so-called adrenal tumours of the ovary is not from adrenal tissue inclusions in the ovary, but from cells in the ovarian mesenchyme itself. This view could obviously be extended to include that vague group of tumours designated by Rottino and McGrath (1939) as masculinovoblastoma, in which there is doubt as to whether the constituent cells are of adrenal or lutein type.

Clinical. The effects of tumours of this group are, as a rule, masculinizing, but in at least a minority of reported cases tumours which histologically conform to this variety have shown no endocrine effect whatever. This has been true in a number of very small tumours, sometimes microscopic in size, and this very factor of size and probably quantitatively slight hormone production would possibly explain the absence of sex changes. It is not so easy to understand why considerably larger tumours may at times show similar hormone inactivity, this being often the case in the small group of highly differentiated neoplasms, especially of the testicular adenoma variety described by Pick (1905). There are some pathologists, like Norris (1938), who question the justifiability of applying the name arrhenoblastoma to tumours which do not actually cause masculinization changes, but it appears wiser to use the pathological structure rather than the clinical effect as a criterion of classification.

The clinical history of such patients is quite characteristic. The first symptoms to appear are not of masculinizing nature, since they simply subtract certain typically feminine attributes from the woman's make-up. In the typical case, a woman who has previously been normal in every way, with normal menstruation and often with a history of one or more pregnancies, ceases to menstruate, shows regression in the size of the breasts, and often loss of subcutaneous fat around the hips, so that her figure becomes less rounded and at times even rather angular. This last mentioned change is naturally inconspicuous in the case of normally thin women.

All of these manifestations are to be looked upon as evidence of defeminization rather than actual masculinization, but they are followed, with some overlapping, by genuine stigmata of masculinization. These are represented by a change in voice,

hirsutism and hypertrophy of the clitoris. The deepening of the voice is due to actual lengthening of the vocal cords and hypertrophy of the laryngeal cartilages. The hirsutism affects the face, extremities, abdomen, buttocks, and perineum, and sometimes the chest and back. Similar hairy overgrowth is not uncommon in women who otherwise are typically feminine, with normal menstruation and fertility, so that hirsutism in itself is not necessarily an evidence of masculinization. In cases of the latter group we must postulate some disorder of the still unknown cortical or hypophyseocortical mechanism believed to regulate hair distribution. But when combined with voice changes and hypertrophy of the clitoris, hirsutism must be looked upon as a part of a masculinization syndrome (Fig. 3).

With removal of an arrhenoblastoma, the symptoms disappear much in the order of their appearance. Menstruation is re-established rather promptly, usually within a month, but in some cases much earlier. The breasts soon regain normal size, and there is a re-deposition of subcutaneous fat about the hips and lower abdomen.

But the positive stigmata of masculinization are more fixed, and they disappear far more slowly and often incompletely. In one of my cases both the voice change and hirsutism disappeared in scarcely more than a year, probably because of the comparatively short duration of the disorder. In another patient, with a longer history, and more pronounced changes, the hirsutism after 2½ years is much less marked, but still a problem, the patient shaving only 3 times a week instead of twice daily, as she did formerly. The voice is still quite deep. The hypertrophy of the clitoris in such cases is also likely to persist, but this is rarely a serious problem, since removal of this organ is so easily done when the overgrowth is very pronounced. This procedure was carried out in the second of the patients mentioned above (Figs. 4 and 5).

All tumours of this group should be looked upon as at least potentially malignant, although recurrences have been reported in only a comparatively small group. This may well be explained by the fact that the rather spectacular clinical history leads to a report of these cases soon after operation, with no later report of the ultimate result. My impression, based on the cases in our own material, as well as those in the literature, is that the recurrence rate will probably approximate 20 per cent, although we hope to have more precise statistics when a larger number of cases is accumulated in the Ovarian Tumour Registry.

The fundamental consideration in discussing the microscopic pathology of arrhenoblastoma is that this represents an imperfect and abortive attempt at the formation of testicular structure. In a minority of cases the microscopic appearance is a reasonable approximation of testicular histology, with the formation of tubules not unlike the seminiferous tubules, sometimes a good reproduction of the rete testis, and not infrequently islands of cells which by their morphology and their lipoid content are identical with the Leydig cells. Arrhenoblastomas of this highly differentiated variety include the so-called testicular adenoma of the ovary described as far back as 1905 by Ludwig Pick, long before the term arrhenoblastoma had been coined (Fig. 6).

At the other extreme there are tumours so highly undifferentiated as to be indistinguishable from sarcoma, although meticulous examination of perhaps many blocks will commonly reveal areas in which the cells are arranged in zig-zag and anastomosing cords which resemble the sex cords of the early embryonic stage of

testicular development. Such tumours may likewise show an occasional tubule, not at all resembling a typical seminiferous tubule, and representing only an exceedingly abortive attempt at formation of the latter (Fig. 7).

The largest number of cases are of so-called intermediate variety, with usually many tubules, numerous sex cords, not infrequently islands of interstitial cells, and a matrix of fibrous tissue of varying degrees of consistency, but sometimes so dense and compact as to resemble fibrosarcoma (Fig. 8).

It is obvious, therefore, that no stereotyped description of the histology of these tumours can be given, and that the term arrhenoblastoma refers to a whole series of histological gradations between the highly differentiated testicular adenoma and the very undifferentiated sarcoma-like variety.

Feminizing Tumours.

As already stated, the primarily testicular scaffolding laid down in the early development of the ovary soon fades out and is followed by a second and typically feminine wave of differentiation, originating like the first *in situ,* as now generally accepted. From the mesenchyme are differentiated broad cords of cells which develop the primitive follicle apparatus. Around each germ cell or oögonium a rosette of satellite cells arranges itself, the future granulosa. We are not here concerned with the origin of the germ cells, and whether they are derived from the germinal epithelium or whether they migrate to the gonadal area by way of a "*Keimbahn*" from a much earlier situs in the hindgut.

According to Meyer's concept redundant rests of granulosa cells are left over in this process of follicle formation, and from such rests tumours may arise in later life. Such tumours, derived from cells already of feminine type, would be expected to exert feminizing effects. The weight of evidence, however, is against the correctness of Meyer's theory of the origin of these tumours. It does not, for example, offer any explanation of the histogenesis of the type of feminizing tumour designated as thecoma. It seems certain that the origin of both granulosa-cell tumours and thecomas must be referred to ovarian mesenchyme, which is the mother-tissue of both granulosal and thecal cells. Tumours arising in this progranulosal and prothecal mesenchyme may be either epithelial (granulosal-cell tumours) or connective tissue (thecoma) in type, or they may be composed of both types of cells (granulosa-thecoma), as they so often are. It must be remembered that in the ovary, as in the genital tract, both epithelium and connective tissue are derived from the same embryonic layer, the mesoderm, so that it is not surprising that there is a greater degree of kinship and probably intermutability between these two types of tissue than pertains to most other areas of the body.

An interesting, but as yet mystifying, observation has been the fact that granulosal and, at times, thecal tumours can be produced in the ovaries of certain animals, especially the mouse, by means of light irradiation, as shown in Figs. 9 and 10. When this observation was made the suspicion was at once voiced that perhaps the same aetiology might be concerned in the human tumours of this group, a suspicion for which there is no substantiation in the previous histories of patients with such tumours. The immediate importance of such studies is that they clearly indicate the mesenchymal origin of these tumours, which may histologically assume granulosal, thecal or lutein characteristics, with usually a mingling of these types.

Another exceedingly interesting but also still unexplained observation is that tumours of this type develop spontaneously

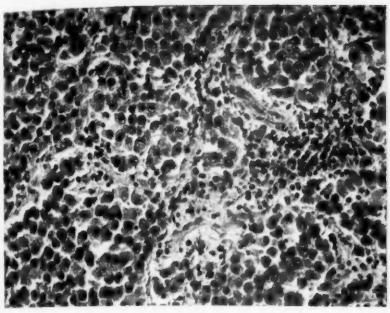

FIG. 1.
Characteristic and not easily mistaken microscopic pattern of dysgerminoma.

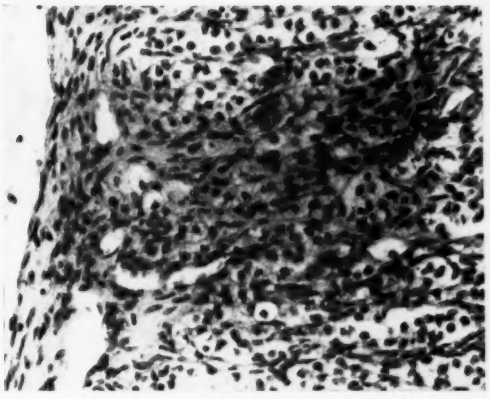

FIG. 2.
Theca-cell changes morphologically resembling adrenal tissue in ovary of infant of one month.

FIG. 3.
Extensive hirsutism in a patient with arrhenoblastoma (author's case).

FIG. 4.
Recent appearance of same patient as shown in Fig. 3. In spite of the fact that she had shaved shortly before being photographed (now shaves three times a week instead of twice daily), her features seem definitely more feminine than formerly.

E.N.

FIG. 5.
Gross appearance of arrhenoblastoma removed from patient shown in Fig. 3.

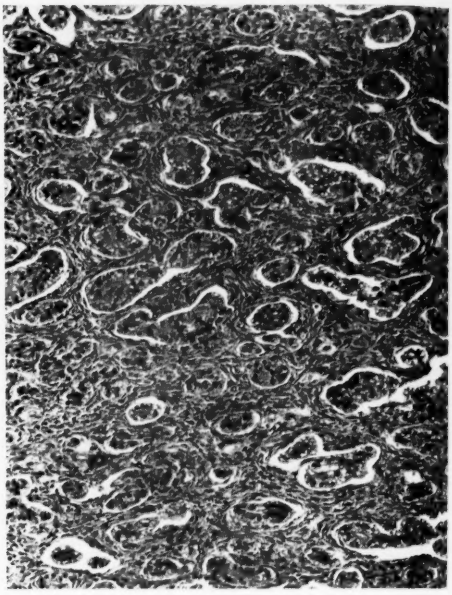

FIG. 6.
Microscopic appearance of arrhenoblastoma showing tubular structure imperfectly suggesting that of testis.

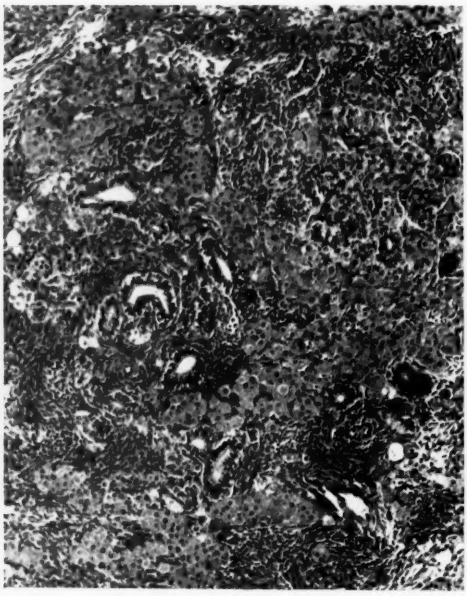

FIG. 7.
Intermediate variety of arrhenoblastoma, showing large fields of pale-staining cells which by their morphology and their lipoid content resemble Leydig cells of testis.

FIG. 8.
Undifferentiated type of arrhenoblastoma showing cord-like arrangement suggesting primitive sex cords.

E.N.

FIG. 9.
Partly luteinized granulosal tumour in ovary of irradiated mouse.

Fig. 10.
Precocious puberal changes, including menstruation, in coloured child aged 7. (Novak, *Textbook of Gynecology*, 3rd edition, 1948, Williams and Wilkins Co.)

FIG. 11.
Puberal appearance of external genitalia in child shown in Fig. 10. (Novak, *Textbook of Gynecology*, 3rd edition, 1948, Williams and Wilkins Co.)

E.N.

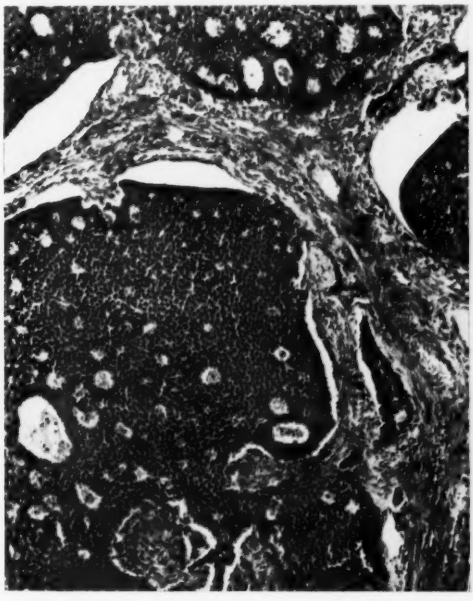

FIG. 12.
Microscopic appearance of granulosa-cell tumour, showing the cluster-like, folliculoid arrangement of the cells and the Call-Exner bodies.

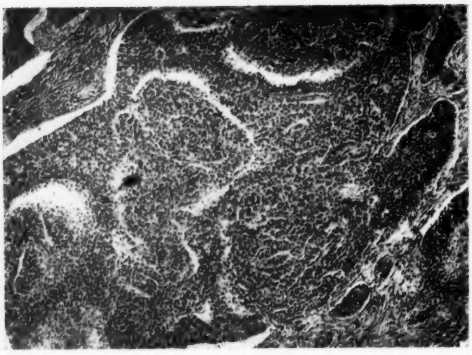

FIG. 13.

Cylindromatous pattern, a very common one with granulosa-cell tumour, although many others are observed.

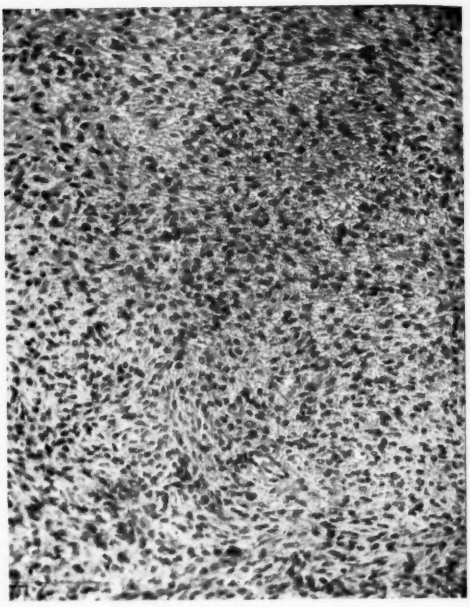

FIG. 14.

Thecoma of ovary.

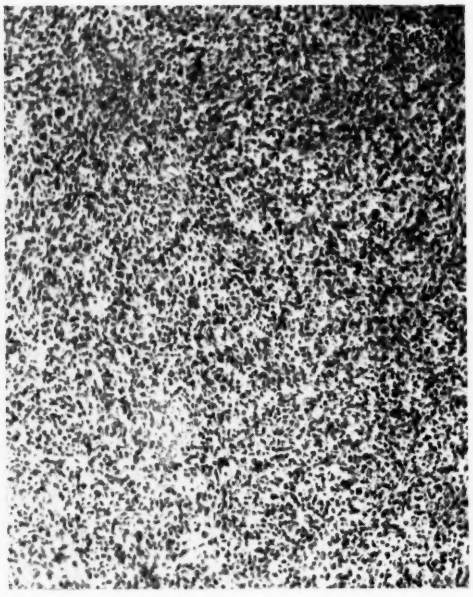

FIG. 15.

Thecoma with admixture of granulosal cells (granuloso-thecoma).

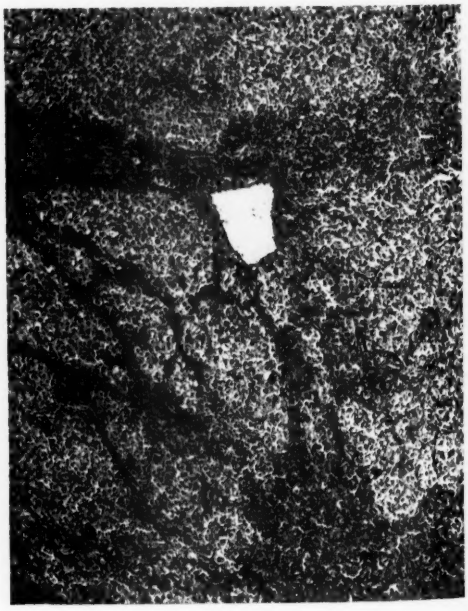

FIG. 16.

Granulosa-cell tumour with extensive luteinization (folliculome lipidique).

in intrasplenic implants of ovarian tissue in castrated animals. The location of such grafts in the spleen makes it quite certain that the oestrogen they produce is destroyed in the liver, according to the best evidence as to the oestrogen-destroying capacity of the liver. Just why this should lead to the formation of granulosa- or lutein-cell tumours is not clear. Various hypotheses have been suggested, such as that the responsible factor is the unopposed action of the FSH principle upon the implanted ovarian tissue. This, however, is an explanation which does not explain, as there is no evidence to suggest that excessive or unopposed gonadotrophic action of this sort can induce tumour formation.

Whatever the explanation may prove to be of these tumours in intrasplenically grafted ovaries, their occurrence again points to an origin from the interfollicular portion of the ovarian mesenchyme, just as was mentioned concerning the tumours produced by irradiation.

Clinical characteristics. The clinical effects produced by the granulosal and thecal group of tumours are just what one would expect if one bears in mind that they produce oestrogen. When they develop in infants or very young children, at a period long before the normal inauguration of the oestrogenic function of the ovary, the clinical picture evoked is that of precocious puberty. The development of the secondary sex characters at normal puberty is unquestionably due to the initiation of oestrogen-production of the ovary (Figs. 10 and 11).

One could expect, therefore, that the production of considerable amounts of oestrogen in a prepuberal child would bring about such puberty changes as development of the breasts, the growth of pubic and axillary hair, a feminine rounding of the body contour, development of the pudenda, hypertrophy of the uterus, and a periodic, menstruation-like type of uterine bleeding. Whether we prefer to call this bleeding menstruation or pseudomenstruation, it is of the purely oestrogen-induced type, and not associated with ovulation. In this important respect the precocious puberty induced by feminizing ovarian tumours differs from the far more common variety designated constitutional. For a fuller discussion of the distinction between the two, as well as of constitutional precocious puberty in general, the reader may be referred to a previous publication by the present author.

The removal of the ovarian tumour producing the precocious developmental changes in young children is followed by a prompt regression of the symptoms, including a cessation of menstruation. The rather spectacular clinical picture in cases of this sort leads to early resort to medical attention, the tumour being practically always small and unilateral. It is not surprising, therefore, that in all such reported cases permanent cure has followed conservative unilateral removal of the adnexa.

When, as is much more common, such an oestrogen-producing tumour occurs during reproductive life, when the menstrual function has long since been established, and all the secondary sex characters long since developed, the effects are simply those which one would expect from a quantitative increase in the circulating oestrogen, much as would be noted after persistent administration of oestrogen. No secondary sex changes would be expected, and none occur. Menstruation may be increased or it may be normal in amount. Disturbances of menstrual rhythm may occur, and even long periods of amenorrhoea are not rare.

Finally, in postmenopausal women, there would again be no especial body changes. The postmenopausal breast is far less sensitive to oestrogen than is the immature

breast of the child, so that no breast changes are noted, nor of course any other general body alterations. However, the uterus, unlike the ovary, retains its sensitivity to hormonal influence after the menopause, so that even in a woman of 70 or 75 years the presence of a granulosal or thecal tumour produces a striking hypertrophic reaction of the normally small senile organ, the hypertrophy affecting both the mucosa and the muscularis, so that the organ may resemble that of a young woman. The endometrium shows the proliferative effect which would be expected from a persistent oestrogen stimulation. This often takes the form of the well-known Swiss-cheese hyperplasia, but in the occasional case the hyperplasia may assume an atypical adenomatous and highly proliferative form, which may be, and undoubtedly often has been, mistaken for adenocarcinoma, as discussed in the recent paper of Novak and Rutledge (1948).

Finally, an increasing number of cases is being reported in which ovarian tumours of granulosal or thecal variety have been associated with unquestioned adenocarcinoma of the endometrium. The relative incidence of this association is too high to avoid the belief that the oestrogen produced by the tumour plays at least a highly predisposing role in the development of the cancer. Aside from the presence of ovarian tumours, there is some evidence to indicate that postmenopausal oestrogen production predisposes to adenocarcinoma. The whole question of the role of oestrogens in the production of cancer is a fascinating and provocative one, but it is too extensive to embark on in this paper.

The special microscopic characteristics of granulosa tumours are the morphological resemblance of the constituent cells to normal granulosal epithelium, and the tendency of the cells to show the growth-pattern of normal granulosa. This is manifested by the tendency of the cells to arrange themselves in small annular clusters or rosettes remindful of the primitive follicular pattern seen in the ovary, and the presence of clear cystic spaces produced by cystic liquefaction of some of the cells; the so-called Call-Exner bodies. There are, however, innumerable architectural patterns which may be assumed by the neoplastic granulosal cells, such as the diffuse, the folliculoid, the cylindromatous, the gyriform, the moiré silk, the pseudo-adenomatous, the tubular, the von Kahlden or folliculoma malignant pattern, and still others. In all these, however, the fundamental granulosal characteristics are discernible, so that in most cases the microscopic diagnosis is not difficult (Figs. 12 and 13).

Thecoma, on the other hand, is made up of bundles of fusiform cells which are apt to be separated by bands of ordinary connective tissue, often hyalinized. The thecomatous cells are usually rich in lipoid. A helpful diagnostic point is that in most cases one sees areas of cells which are typically or approximately granulosal in appearance, emphasizing the fact that the descendants of the feminine mesenchyme may assume either granulosal or thecal characteristics, or that there may be a mixture of both. There are frequent instances in which the tumour is better spoken of as granuloso-thecoma rather than either granulosa-cell tumour or thecoma. By means of reticulum stains of one sort or another, it is possible to distinguish the granulosal and thecal cells with fair precision, but there is usually very little difficulty on this point merely from the morphology of the cells (Figs. 14 and 15).

Both granulosal and thecal-cell tumours may undergo interesting cell changes in the luteinization, partial or complete, which the granulosal or thecal cells, as the case may be, may undergo. Such a change is more

often seen with the granulosal type of tumour (the *folliculome lipidique* of Lecene). In spite of this luteinization, and even when this is quite extensive, the biologic effects of such tumours are usually those referrable to oestrogen alone, so that the transformation of the granulosal into lutein cells appears to be a purely morphological one rather than actually functional (Fig. 16).

But there are exceptions to this, for in at least a small group of reported cases, including two of my own, both oestrogen and progesterone effects were noted. For example, in one of my cases a partially luteinized thecoma in a woman of 54, ten years beyond the menopause, was associated with a definite progestational endometrium. In some cases the lutein transformation of a granulosal tumour is complete, and it is to this type of lesion that the term luteoma is, in my opinion, best applied. In a case of this sort observed by Henriksen, who kindly sent me material for study, the endometrium exhibited typical decidual transformation.

The term luteoma has been a very controversial one, and certain masculinizing tumours have been reported under this designation. However, I believe that the lutein-like cells characterizing such tumours are really of adrenal character, or that they are derivatives of the totipotent mesenchyme, as I have previously discussed. It is difficult to believe that neoplasms could arise directly from such transitory and short-lived elements as lutein cells, which, after all, are only modified granulosal or or thecal cells. In the present state of our knowledge it would seem best to limit the term luteoma to this feminizing group, and to avoid its use for masculinizing growths.

Other considerations. I have said nothing as to the possible value of hormonal determinations in the diagnosis of these tumours, because little of a definite nature can be said. Observations on this point have been meagre, especially in the case of the masculinizing tumours, and difficult to evaluate because of lack of standards in technique. A curious and unexplainable finding in a small number of dysgerminomas has been a positive biological pregnancy test, at least suggesting that the tumour may produce gonadotrophes.

Nor have I discussed the so-called gynandroblastomas, in which one and the same tumour shows a combination of typical granulosa-cell and arrhenoblastomatous elements. I have had the opportunity of studying 4 of these cases. Plate collected 11 from the literature, but an analysis of these would seem to eliminate a good many as faulty interpretations. In the majority of such cases the effect of the combined tumour has appeared to be masculinizing.

Finally, I have gone into little detail as to the incidence of recurrence and metastasis after the removal of tumours of this group. All of them must be looked upon as potentially malignant, though the degree of malignancy is certainly far less than with the ordinary types of primary ovarian carcinoma. Only a few follow-up studies of the various forms have been made, usually of comparatively small groups. The most recent of these, dealing with dysgerminoma, is that of Santesson (1947), which conforms to my own conviction that pathologists are inclined to view these tumours, as well as others of this dysontogenetic group, somewhat too lightly. In 24 of 28 cases in which rupture of the capsule had occurred preoperatively, including some in which the operation was of radical type, recurrence occurred, with a fatal termination within 5 years. On the other hand, in 61 patients in whom the capsule was still intact, there was a 5-year survival in 49.

With granulosa-cell tumours, as with the

other two types which have been discussed, I believe that as more extensive follow-up studies become available the incidence of recurrences and metastases will be found to be much higher than the low figure now given by some authors, probably somewhere between 20 and 25 per cent. It must be remembered that recurrences may be late, as much as 18 years after the original operation. The same general comment may be made as to arrhenoblastoma, in which follow-up studies are even more scant than with the other two varieties.

SUMMARY.

The present paper is based on the correlated pathological and clinical study of 43 cases of dysgerminoma, 51 of arrhenoblastoma, and 161 of granulosa-cell tumour and thecoma. The probable origin of dysgerminoma from cells dating back to the early undifferentiated stage of gonadal development explains why this tumour-type produces no endocrinal effects.

As regards masculinizing tumours, our ideas as to this histogenesis show an increasing departure from Meyer's simple concept of an origin from vestiges of masculine-directed cells persisting in the medullary portion of the ovary. This would still seem adequate in the explanation of arrhenoblastoma, a designation which includes all possible histological gradations of testicular structure-reproduction, always imperfect and often so highly abortive as to be almost unrecognizable. The theory does not, however, explain the masculinizing groups spoken of under such designations as virilizing lipoid tumour, adrenal-cell tumour, masculinizing luteoma, and masculinovoblastoma. These seem better explainable by invoking the factor of the differentiating potency of the gonadal interfollicular mesenchyme, as has been discussed in the paper. It seems probable that the histogenesis is a varied one, and that at least some members of this group are of definitely adrenal character, with a probable origin from adrenal-cell embryological inclusions in the ovarian area.

The increasing accent on the role of the mesenchymal differentiating potency has been exemplified also in the explanation of the histogenesis of granulosal- and thecal-cell tumours. Meyer's theory of an origin from granulosal-cell rests seems inadequate, and we must go back to a progranulosal and prothecal mesenchymal phase for the explanation of the feminizing tumour. Such tumours may develop along either epithelial (granulosal) or connective tissue (thecal) lines, but they often show a mixture of both, justifying the designation of granuloso-thecoma. Perhaps a more inclusive designation for the whole group would be feminizing mesenchymoma. The not uncommon luteinization of these tumours is usually partial, but in the occasional case is complete, in which case the term luteoma has its clearest justification. In the present state of our knowledge it is unwise to apply this name to any of the masculinizing group of tumours.

Finally, the clinical characteristics of tumours of the above-mentioned groups have been discussed, with chief reference to their endocrine effects.

The appended bibliography includes not only papers referred to in the text, but also a selected list of others bearing on the general subject.

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PRIMARY CARCINOMA OF THE VAGINA*

BY

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PRIMARY cancer of the vagina is a rare disease—much more rare than secondary cancer—and on that account it must have an appeal at least to the curiosity, but more than that, a study of the literature of the subject reveals a state of almost universal despondency. In 1935 Frederick Joseph Taussig, who made so many advances in the treatment of gynaecological cancer, addressed these words to a Congress organized by the American College of Surgeons: "We acknowledge our total inability to do anything effective for primary cancer of the vagina."

I am convinced that the comparative rarity of this disease is responsible to some extent for the almost universally gloomy outlook, since few can get sufficient material and gain enough knowledge of the behaviour of the disease to become proficient in its treatment.

Since an increasing number of cases of vaginal cancer were being referred to me for treatment under the aegis of the recently-formed North of England Cancer Organization (there were 10 in 1947 which are not included in this paper), I determined to make a study of our own experiences in Newcastle and to analyze our failures and successes in order to see if I could get a clearer knowledge of the disease and its behaviour, and thus form a basis for future treatment. It is largely the results of this analysis which I wish to communicate to you this afternoon.

It is now 122 years since Cruveilhier first described primary cancer of the vagina before the Anatomical Society of Paris in 1826, but it was certainly known, if not reported, before that time, for he stated in his paper that "the association of a cancerous vagina with a normal cervix and uterine body is not rare." How rare it is in relation to the population as a whole we cannot determine. We cannot even determine how frequently it is a cause of death, for the Registrar-General makes returns of carcinoma of the vulva and vagina under one heading, and one assumes that his returns are accurate. As to their accuracy you can judge for yourselves when I tell you that the office of the Registrar-General recently supplied me with the dates and cause of death of 136 patients who had suffered from carcinoma of the vulva, and 47 of these had been discharged from hospital with untreatable disease confirmed by biopsy, and all had died in a few months, yet in 32 of these cases the certified cause of death was not cancer of the vulva but a variety of conditions ranging from cancer of the uterus to senility and syphilis.

The best that can be done is to establish an incidence in relation to other forms of malignant disease and Table I shows this incidence during the last 16 years at Newcastle. This figure of 44 may be a slight underestimate as I have rejected, for the purpose of this paper, 10 cases in

* The Tenth William Blair Bell Memorial Lecture delivered before the Royal College of Obstetricians and Gynaecologists on 23rd January, 1948.

TABLE I.
Total Cases of Malignant Disease of the Female Genital Organs, 1930–1946.

Carcinoma of cervix uteri	1960
Carcinoma of ovary	386
Carcinoma of vulva	188
Carcinoma of corpus uteri	155
Carcinoma of vagina	44
Carcinoma of Fallopian tube	1
	2734

Ratio of carcinoma of vagina to carcinoma of cervix, 1 to 45.
Ratio of carcinoma of vagina to genital carcinoma, 1 to 62.

which, either from the paucity of the notes or on account of the advanced stage of the disease, it was not clear that they were actually primary vaginal cancers. Thirty-six came at some stage or other under my own observation. The cases under consideration were all quite clearly associated with a normal uterus and vulva, and can be regarded as genuine cases of primary vaginal carcinoma. Its frequency in relation to carcinoma of the cervix I have found to be 2.2 per cent, a figure which is closely comparable to Elizabeth Hurdon's estimate (1942) of 1.9 per cent at the Marie Curie Hospital.

TABLE II.
Age Incidence.

Age group	No. of cases	Age group	No. of cases
0–20	0	51–60	16
21–30	1	61–70	7
31–40	4	71–80	4
41–50	12	Over 80	0

Average age, 54.
Youngest, 24.
Oldest, 73.

Age incidence (Table II). There is a considerable difference of opinion among various authors as to the commonest age at which this disease occurs. Elizabeth Hurdon asserts that it is a disease of advanced life, and that only 2 of her patients were under 50. Emmert (1938) found an average age of 53; Moench (1931) an average age of 59; den Hoed (1936) had 10 cases under 50 and 17 between 50 and 69. At the other extreme Novak (1940) believes the commonest age-group to be 35 to 55, and Ewing (1940) places the figure as low as 30 to 40. As will be seen from Table II the average age in my series is 54, with 40 per cent of the patients under the age of 51. It is clear therefore that there can be no justification for the attitude taken by some that the age incidence is so high and the expectation of life so short that the time spent in achieving a cure is not justified.

Parity and civil state (Table III). Nearly a quarter of these patients were nulliparous and, in this respect, carcinoma of the vagina

TABLE III.
Parity and Civil State.

Civil state:	Married and widowed	39
	Single	4
	Not stated	1
Parity:	Parous	29
	Nulliparous	7
	Not stated	8

seems more closely allied to carcinoma of the vulva than to cervical tumours. One of these tumours arose during pregnancy but, owing to delay in diagnosis, treatment was not instituted until 6 months after delivery.

Symptomatology (Table IV). As in carcinoma of the cervix, bleeding is also the

TABLE IV.
Symptoms.

Vaginal bleeding	24
Brown or red discharge	8
Pain and bleeding	3
Post-coital bleeding	2
Postpartum bleeding	1
Pain	1
No symptoms	1
No information	4

predominant symptom in carcinoma of the vagina. Bleeding cannot take place until ulceration occurs and, since the vagina is a very thin structure in comparison with the cervix, it might be expected that this symptom would be noticed earlier in vaginal cancer. Of 38 cases in this series bleeding had been present for 3 months or less in 20. Early diagnosis ought to be possible but the very thinness of the vaginal wall, which might be expected to allow symptoms to develop early, also allows the growth to spread to neighbouring structures at a very early stage and some very advanced cases were encountered who had had symptoms for only a few weeks. (Table V.)

TABLE V.

Duration of Symptoms.

	No. of cases	No. of untreatable cases
No symptoms	1	0
Less than 1 month ...	2	1
1–3 months	17	3
4–6 months	10	2
7–9 months	3	2
10–12 months	3	0
13–15 months	1	1
16–18 months	0	0
19–21 months	0	0
22–24 months	1	0
No information	6	2

Pathology. Concerning the histological appearances of vaginal carcinoma there is no difference of opinion among writers on the subject. All are agreed that the vast majority of these tumours are squamous-celled carcinomas. The occasional appearance of primary adeno-carcinoma of the vagina gives rise to interesting speculation concerning its development. These tumours most probably arise from Müllerian rests, and in this connexion I would like to draw your attention to a rather uncommon disease first described by Bonney and Glendinning (1910) and termed by them adenomatosis vaginae. They described a patient in whose vaginal wall were multiple mucus secreting glands which had coalesced and formed small cysts. This disease was more fully dealt with in 1940 by Plautt and Drayfuss, of New York, who described a further stage in which there was a cauliflower-like red mass clinically indistinguishable from carcinoma, and they believe that this condition is the forerunner of most cases of primary adenocarcinoma of the vagina. It certainly appears to have been in one of my cases. This tumour occupied the whole of the anterior vaginal wall and obstructed but did not invade the urethra. It was at first thought to be secondary to a corporeal or bowel tumour, but exhaustive investigations did not reveal the presence of any such primary. I transplanted the ureters and at that time was able to confirm the absence of an intestinal carcinoma. I followed this by excising the cervix, vagina, urethra and bladder base by the perineal route and the patient is in excellent health one year after operation.

One other case of primary adenocarcinoma occurred in this series. This tumour occupied the upper third of the posterior wall of the vagina and contained corpora amylacea such as are found in the prostate and was undoubtedly derived from a Wolffian remnant. The outcome of this case was not so happy, as I accidentally wounded the rectum in performing Wertheim's operation and the patient died of peritonitis.

It has been suggested that carcinomas of the vagina are generally more malignant than those of the cervix and Mary Moench found at the Mayo Clinic that 20 out of 35 cases were of Broder's Grade IV, that 12 were Grade III, 2 of Grade II, and only one of Grade I. Emmert, on the other hand, in 13 cases found 8 of Grade II and 5 of Grade III, and none in Grade IV.

Dr. Glucksmann, of Strangeways Laboratory, Cambridge, has classified 27 of the cases in my own series from which material has been available with the results shown in Table VI. In addition he has classified them into anaplastic squamous (and this term, as used here, signifies a tumour in which there is a low degree of differentiation in the growing edge but which on becoming old may show a high degree of keratinization, even with cell-nest formation) and anaplastic parkeratotic which are undifferentiated tumours. Judging from

TABLE VI.
Histological Classification.
(27 sections only available for study.)

Broder's Grade	No. of cases
1	1
2	6
2–3	8
3	11
3–4	1
4	0

" Anaplastic squamous "	8
Anaplastic parkeratotic	17
Adenocarcinoma	2

work on carcinoma of the tongue and cervix a high proportion of tumours which respond unfavourably to radiotherapy are found in this latter group and it is also probable that this type of tumour is associated with early and often widespread involvement of the regional lymphatics. Any further sub-division of this small series of cases becomes mere speculation and is not profitable.

Pathological anatomy. The anatomy of the vagina and its lymphatics is an important matter in the approach to this problem but it is necessary to reduce it to simple terms.

The vagina must be regarded as a tube open at its lower end and closed by the cervix at its upper end. Lying behind it is the rectum and in front the urethra and bladder. At each side is a thick band of connective tissue, the paravaginal tissue, merging with the suspensory ligaments of the cervix above and the levator ani muscles below.

The lymphatics of the vagina follow the relatively simple arrangement shown in Fig. 1. Those from the upper half drain to the inter-iliac nodes lying between the external and internal iliac arteries, and to the internal iliac nodes, and generally follow the course of the lymphatics of the cervix. Those of the lower end drain into the inguinal lymphatics, but some drain directly into the medial group of external iliac nodes. There is a free anastomosis between the lymphatics of the upper and lower half of the vagina and also between those of the right and left sides. In considering the lymphatic spread of vaginal tumours, the vagina can be divided into thirds. Tumours of the upper third metastasize in the same way as a cervical cancer, those in the lower third in the same way as a carcinoma of the vulva, whilst those occupying the middle third spread their metastases by both routes. A close understanding of this relatively simple arrangement is absolutely necessary as a basis of treatment.

Neighbouring structures. The proximity of the urinary apparatus and rectum proves an obstacle in treatment, although this is more apparent than real. Our minds tend to be fixed too much on the more common carcinoma of the cervix, so that when we meet a small carcinoma of the vagina involving the bladder we tend to think of it as being hopelessly advanced. Now this is not always the case. As I have pointed out before the vaginal wall is very thin and involvement of the urethra, bladder and rectum may occur at an early stage in the development of the growth, whereas, owing to the size of the cervix, fistula-forming in growths of the organ are almost invariably associated with wide-

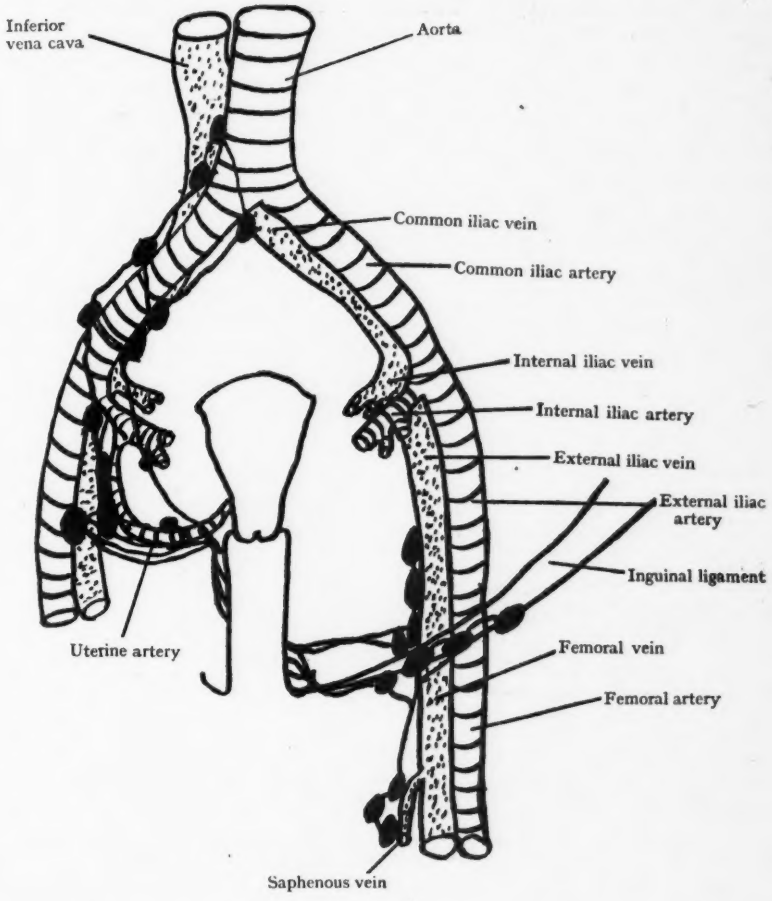

FIG. 1.
Schematic representation of the lymphatic drainage of the vagina.

spread involvement of the broad ligaments and pelvic cellular tissues. One of the untreated cases in this series had a small ulcer the size of a sixpence at the lower end of the anterior vaginal wall which had perforated the urethra in 2 places. This patient did not die until 2 years after she had been rejected as too advanced for treatment, whereas the average survival after rejection was 10 months, or 9 months if this particular case is rejected from the series. None of our cervical cases, rejected because of fistula formation, survived more than 4 months. Preliminary transplantation of the ureters will give greatly increased scope for either surgery or radiotherapy in such cases. Another patient in this series had a tumour on the posterior vaginal wall attached to the rectal mucous membrane. The tumour and the rectal mucosa were removed and the patient is now alive and well 9 years after operation.

Abnormal anatomy. There does appear to be an increased incidence of carcinoma of the vagina in women with prolapse, especially if they have worn pessaries. There were 3 such cases in this series and one in a woman with a huge procidentia (Plate I). In one case a carcinoma had developed in the left lateral fornix where this had been in contact with a large fibroid polypus.

Situation of the tumour. Table VII shows the situations in which the tumours were encountered in this series and gives some idea of the problems facing one when an attempt is made to design a radium applicator for the treatment of vaginal carcinoma. The majority of these tumours are said to arise on the posterior wall. Emmert found 14 out of 37 in that situation; Rhode (1897) 71 out of 123 cases; den Hoed 12 out of 31; and Mary Moench 65 per cent on the posterior wall and 17.5 per cent on the anterior wall. In my series the posterior wall was involved in 23 cases, but where only one wall was attacked it was the anterior that was most frequently the site of the tumour. In the Mayo Clinic series 92 per cent of the posterior wall tumours occurred in married women, whereas in single women 47 per cent of the tumours were on the anterior wall, but in my series all the anterior wall tumours were encountered in married women. Once again it is the rarity of the disease and the small series that are responsible for such wide variations in the figures.

Treatment. For many years no real attempt was made to treat vaginal cancer, indeed, for long after its original description, no treatment was possible. The dawn of antiseptics was not yet, abdominal surgery was an art of which few dreamed, and Pierre and Marie Curie were unborn. As late as 1886 we find Herman purposely creating a vesico-vaginal fistula to relieve retention in such a patient, and 10 years later C. H. Roberts was considered exceedingly bold in advocating attempts at extirpation of certain small vaginal cancers; for anything more advanced he advised cautery, scraping and the use of antiseptic tampons. In the same discussion Lewers (1896) stated that in his opinion operative treatment of all kinds was useless.

TABLE VII.
Situation.

	Upper third	Middle third	Lower third	Upper and middle thirds	Middle and lower thirds	All thirds	Total
Anterior wall	1	3	4	1	1	3	13
Anterior and right lateral	0	0	0	0	1	0	1
Anterior and left lateral	0	0	0	0	0	1	1
Posterior wall	4	1	2	1	0	1	9
Posterior and right lateral	1	0	0	[illegible]	0	0	1
Posterior, right and left lateral	0	0	0	1	0	2	3
Posterior, anterior and left	1	0	0	0	0	1	2
Encircling vagina	0	0	2	3	0	3	8
Right lateral	1	1	1	0	0	0	3
Left lateral	2	0	0	1	0	0	3
	10	5	9	7	2	11	44

Anterior wall not involved, 19 cases.
Posterior wall not involved, 21 cases

At Leicester in 1905 Ernst Wertheim introduced his radical operation for carcinoma of the cervix to this country, and after a while certain operators commenced to use it as a method of treating some vaginal cancers, and in 1923 we find three papers in the *Journal of Obstetrics and Gynaecology*, by Dougal, Holland and Stevens, describing cases treated in this manner. Meanwhile radium was being more extensively used for both cervical and vaginal cancers and it is of some interest to note that the first suggestion for the use of radium in the treatment of internal cancer, as opposed to skin cancer, came not from a doctor, but from Alexander Graham Bell, the inventor of the telephone, who suggested it to a friend, Dr. Zowers (1903). However, neither method was meeting with much success, as Stevens remarked in 1923 that the tumours are difficult to treat surgically and the results have been very bad, whilst in 1931 de Buben, in Budapest, collected the published results of 129 cases treated by radium with a 5-year cure rate of 4 per cent. Hopes were temporarily raised by the treatment of cancer with lead, but as far as I can discover Blair Bell (1930) treated only one case of vaginal cancer solely in this manner and that was a secondary tumour. Professor Jeffcoate (1947), who has kindly searched the collected papers of Blair Bell in the possession of Liverpool University, informs me that Blair Bell favoured excision of the uterus, appendages and vagina from below and followed this by lead treatment. He seems, however, to have made no specific contribution to the literature on this subject. No one has ever published anything approaching a series of cases of carcinoma of the vagina treated by radical surgery, but there is no doubt that the operation is a much more difficult one than when performed for carcinoma of the cervix.

Naturally enough when considering radical surgery in genital cancer the name of Victor Bonney comes to mind. Mr. Bonney has been kind enough to send me a note on his experiences with this disease. Few of the patients that he saw were operable, mostly because of the tumours having involved neighbouring structures, due to the thinness of the vaginal wall. He further states that "most of the primaries that I have seen were high up in the vaginal wall and curiously enough in young women. . . . I remember one remarkable case in a girl of 19, but it was absolutely inoperable". He used Wertheim's operation on only a few occasions but there is unfortunately no record available of these particular cases.

With so many difficulties besetting surgical treatment and with gradually improving results in the treatment of cervical carcinoma with radium it is easy to see how radiotherapy came to take pride of place in the treatment of carcinoma of of the yagina, but the results in general fall short of expectation, and here once again we find the infrequency of the disease embarrassing the radiotherapist just as it does the surgeon. Emmert of St. Louis recorded an absolute 5-year cure-rate of 12 per cent; den Hoed from Amsterdam, a relative 3-year figure of 30 per cent. The Mayo Clinic figure is 17 per cent absolute, while 12 per cent is the result for the treatment of 99 cases at the Memorial Hospital, New York. Berven and Heyman (1939), from Stockholm, reported seven 5-year cures out of 53 cases, and the only encouraging results are those of Courtial (1939) at the Paris Radium Institute, who recorded ten 5-year survivors out of 22 cases treated between 1919 and 1933. Lederman and Meyneord (1942) were able to find only 7 cases at the Radium Department of the Royal Cancer Hospital between 1929 and 1940. Most of them were advanced and

there was one 5-year survivor. It is not easy or profitable to draw conclusions from the relatively small series reported in the literature, but when I came to make a detailed analysis of the results of treatment in our own cases at Newcastle I found many points of interest which explain some of our past failures, and I will now discuss in detail the results of the 44 cases which have been seen between the years 1930 and 1946.

Methods of treatment and results. Eleven patients were considered too advanced for treatment and of the remaining 33, 6 were treated surgically and 27 by radium.

Untreated cases. The average duration of life in these cases was 15 months from the onset of symptoms and 10 months from the time that they were rejected as unsuitable for treatment. Table VIII shows a summary of these patients and the reasons why they were not treated. Some of them survived so long that they were almost certainly treatable, and I think that we have rejected a number of them without justification, and particularly where small tumours involved the bladder. We have rejected these because of a lack of vision concerning the possibility of employing surgery to help us over our difficulty with these important neighbouring structures.

Surgery (Table IX). There were 6 cases treated purely by surgery. Three were not particularly extensive operations and 3 were very radical. Let us consider first the less radical operations. One consisted of an excision of the lower half of the vagina with dissection of the superficial groin-nodes and the patient died 6 months later with a local recurrence and secondaries in the mediastinum. One is surviving 14 years after a local excision of the tumour and another 9 years. Of the 3 radical operations, I have already mentioned 2 as they were performed for the 2 adeno-carcinomas that occurred in the series. The third was a squamous-cell tumour, not very extensive, but involving the base of the bladder. I transplanted the ureters and then performed a radical hysterovaginectomy with total cystectomy by a combined abdominoperineal approach. The pelvic nodes which were removed showed no evidence of growth. This patient was an extremely difficult individual, who was pugnaciously antagonistic to the nursing staff. She developed a bed-sore over her sacrum, upon which she insisted on lying.

TABLE VIII.

Summary of Untreated Cases.

Case No.	Age	Duration of symptoms	Reason for rejection	Survival after rejection
2	50	3 months	Urethra destroyed	12 months
3	65	6 months	Urethra involved	24 months
5	53	2 months	Extensive disease	8 months
6	73	1 month	Cardiac disease	3 months*
11	48	Not stated	Tumour fixed to bone	7 months
13	71	15 months	Advanced age	6 months
15	60	Not stated	Extensive disease	6 months
24	54	2 months	Urethra destroyed, tumour fixed to bone	6 months
27	49	4 months	Bladder involved	6 months
28	59	7 months	Extensive disease	10 months
30	59	9 months	Paravaginal tissue fixed to pelvic wall	15 months

* Death from coronary thrombosis.

TABLE IX.

Cases Treated by Surgery.

Case No.	Site of tumour	Nature of operation	Survival	Condition on death
4	Lower third 4 walls	Excision and superficial groin dissection	6 months	Local recurrence and widespread metastases.
7	Lower third 1 wall	Local excision	14 years	(Still alive and well.)
20	All thirds 1 wall	Local excision	9 years	(Still alive and well.)
26	Middle third 1 wall	Ureteric transplant Wertheim's hysterectomy and total cystectomy	6 months	Osteitis of the sacrum. No recurrence.
29	Upper third 1 wall	Wertheim's hysterectomy	0 months	Peritonitis. Post-operative death.
43	Middle and lower thirds 1 wall	Ureteric transplant Vaginectomy and urethrectomy	1 year	(Still alive and well.)

When I made her walk about all day she discharged herself from hospital, and at home, despite the protests of her doctors and relatives, she lay on her back and refused to get out of bed. She died of osteitis of the sacrum 6 months after operation with no evidence at autopsy of recurrence or metastases.

Radium. Twenty-seven cases were treated with radium. There was 1 post-operative death; 1 patient died of intercurrent disease and 16 of cancer before 5 years had elapsed. Of the remaining 9, 1 is alive and well after 1 year, and 7 are surviving 2, 3, 4, 8, 9, 10 and 13 years respectively, whilst another died of intercurrent disease 11 years after treatment. The gross results of cases treated more than 5 years ago are seen in Table X. It will be noted that the 10-year figures are slightly better than the 5-year results. This is due to chance playing a hand in a very small series of cases. As it happens, in the 10-year figures there are quite a number of cases that have done well with radium throughout the series, namely tumours of the upper vaginal third. In the subsequent group there were not so many of these, and this explains the freak result. If we exclude tumours of the upper third of the vagina it is not an easy matter to apply radium to those occurring elsewhere, and also to ensure that it stays in the proper position during treatment. When one considers the diversity of situations in which a growth may be found, and the rarity with which the disease appears, it is not surprising that the odd case which is seen from time to time is made to conform to one of the often-used methods, such as one of the cervical techniques, sometimes

TABLE X.

Results of Radium Treatment.
(Various techniques)

Total cases seen	Total cases treated	Total cases alive	Total cases dead
	10-year cases.		
14	7	3	4
	*5-year cases.**		
25	14	5	9

* Includes 10-year cases.

with little or no modification. Lederman and Mayneord hinted at this when they said "because of the relative rarity of the disease it is doubtful if any one radiotherapeutic centre has had sufficient experience to develop and perfect a reliable technique," and they further added "that in cancer of the upper third the ordinary cervical technique is reliable but it is not an easy matter to apply radium to a tumour in the lower two-thirds of the vagina."

In our attempts to get accurate irradiation of the tumour we used interstitial radium on 7 occasions and there was one postoperative death (Table XII). One patient died one year after treatment from other causes and none of the others survived longer than 2 years. This method can only be compared to a local excision and therefore cannot be expected to give more than an occasional success. I cannot believe that there is anything to commend it as a routine measure. It has solved one problem only, namely the local irradiation of certain awkwardly-placed tumours, but it has left unsolved the problem of dealing with the neighbouring parts of the vagina and paravaginal tissue.

For many years we employed the Stockholm technique in dealing with cases of cervical cancer and more recently the Manchester technique, and it was natural that we should employ some modification of these methods in the occasional vaginal carcinoma which we encountered. You will see from Table XII that the results

TABLE XI.
Interstitial Radium.

Case No.	Site of tumour	Survival	Condition at death	Duration of symptoms
8	Middle third 1 wall	7 months	Local tumour present	3 weeks
9	All thirds 3 walls	3 months	Local tumour present	Not stated
12	Upper third 1 wall	11 months	Pelvic gland metastases	Not stated
34	Lower third 1 wall*	25 months	Metastases in liver	1 year
38	Lower third 4 walls	12 months	No growth. Died of other causes	None
40	Middle and lower thirds 1 wall	8 months	Fungating groin glands	6 months
41	Middle and lower thirds 1 wall	0 months	Postoperative death Pulmonary embolus	6 weeks

* Groin dissection in addition to radium.

TABLE XII.

Manchester Cervical Technique.
Total cases treated, 6

Died at 2 years	1
Died in less than 1 year	2
Alive and well after 4 years	2
Alive and well after 2 years	1

Stockholm Cervical Technique.
Total cases treated, 12

Alive and well more than 10 years	2
Alive and well 1 year	1
Alive and well more than 5 years	2
Died other causes after 10 years	1
Died in 1 year	6

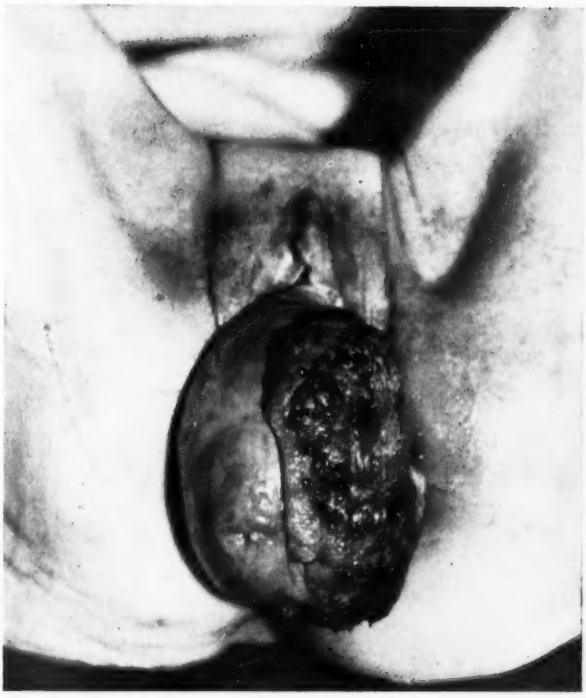

PLATE I.
Procidentia associated with vaginal Carcinoma.

S.W.

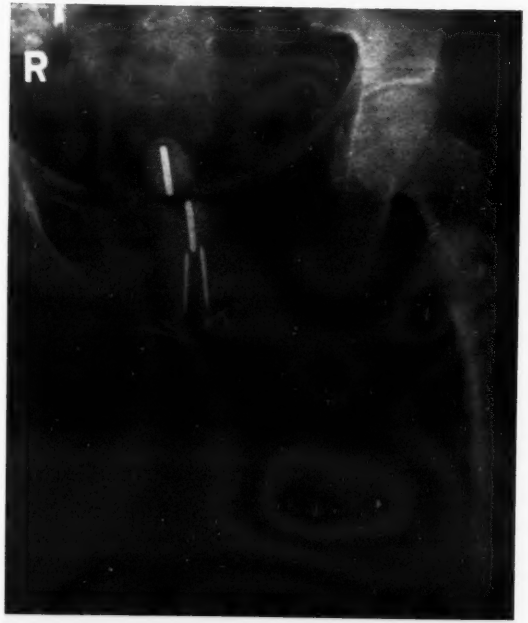

PLATE II.
Radiograph showing radium imbedded in stent in correct position.

PLATE III.
Radiograph showing radium imbedded in stent in incorrect position.

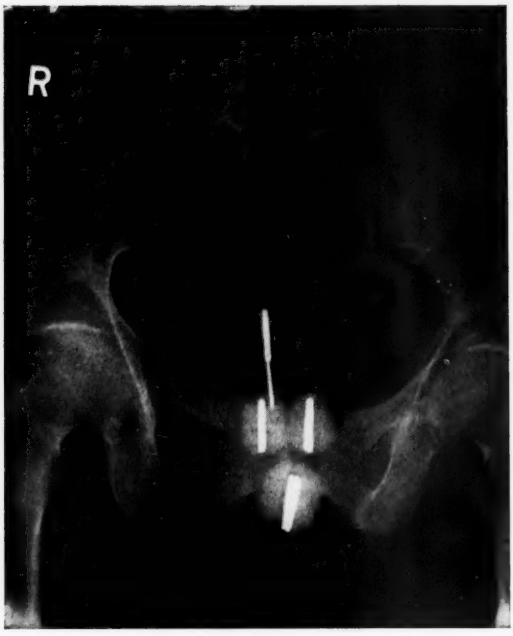

PLATE IV.

Radiograph showing arrangements of " ovoids "
to treat carcinoma of the vagina.

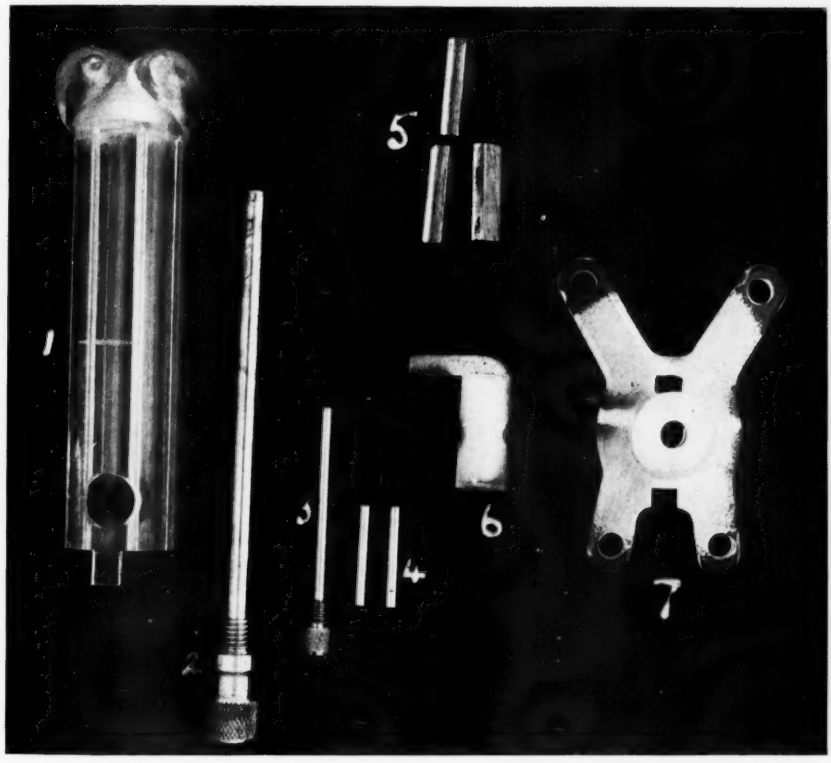

PLATE V.

Key to Plate:

1. The vaginal tube with ovoids attached at the upper end.
2. The central radium container.
3. Pin for closing central radium container.
4. Brass blanks for central radium container.
5. Three segments of lead screen.
6. Clamping pin for stabilization of harness attachment.
7. Harness attachment.

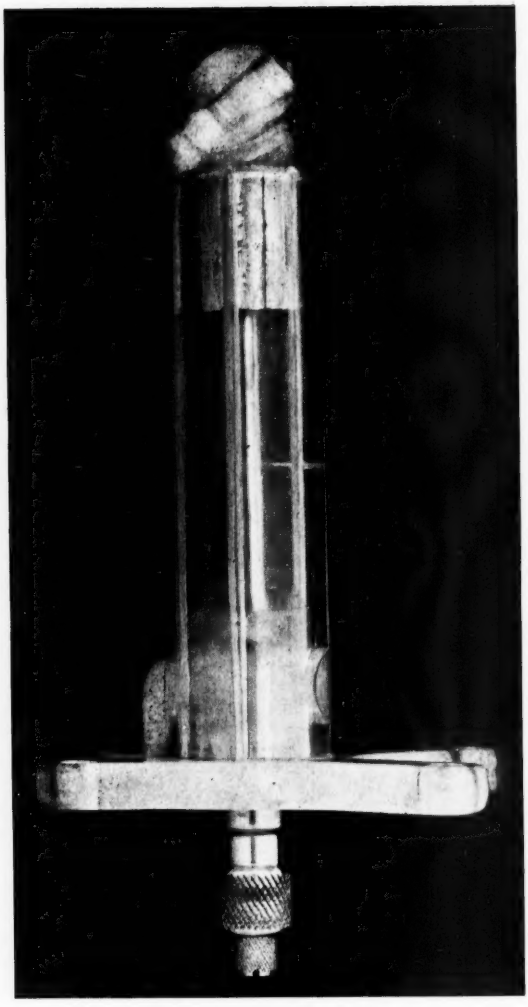

PLATE VI.
The assembled applicator.

PLATE VII.
Radiograph of vaginal applicator *in situ*.

from the Stockholm technique in which all the earlier cases figure are a curious mixture of dismal failure and brilliant success. The Manchester technique has been used only in the last 5 years but looks as though it may well follow along the same lines.

If you turn to Fig. 2 you will see superimposed on a diagram of the uterus and vagina an area of effective irradiation resulting from the arrangement of radium designed to treat a cervical cancer. By an area of effective irradiation I mean an area in which we believe that it is possible to deliver a dose lethal to cancer from the arrangement shown. It at once becomes apparent that tumours situated in the middle and lower thirds of the vagina will receive so little irradiation that they cannot be cured unless extra radium sources are added.

Table XIII shows our results in 11 cases in which, either on account of the tumour being situated in the upper vaginal third, or because we added an additional radium source, adequate irradiation was given by an intracavitary method. Six of these 11 patients are living or have lived more than 4 years. Table XIV, on the other hand, gives the results of 7 cases treated by an unmodified cervical technique in which the tumours did not wholly lie in the upper third of the vagina. The very fact that I have used the words months instead of

TABLE XIII.
Results of Radium Treated Cases where the Growth was Adequately Irradiated.

Site of tumour	Survival	Condition at death	Technique
Upper third 1 wall	11 years	Died other causes	Stockholm
Upper third 1 wall	13 years	(Still alive and well)	,,
Upper third 1 wall	10 years	(Still alive and well)	,,
Upper third 1 wall	9 years	(Still alive and well)	,,
Upper third 2 walls	1 year	Local recurrence, pelvic gland and liver metastases	,,
Upper and middle thirds 1 wall*	8 years	(Still alive and well)	,,
Upper third 1 wall	1 year	(Still alive and well)	,,
Upper third 3 walls	4 years	(Still alive and well)	Manchester
Middle third 1 wall*	4 years	(Still alive and well)	,,
Upper third 1 wall	2 years	Pelvic gland metastases	,,
All thirds 4 walls*	2 years	(Still alive and well)	,,

* Additional radium added to cover whole tumour.

TABLE XIV.

Results of Radium Treated Cases where the Growth was Inadequately Irradiated.

Site of tumour	Survival	Condition at death	Technique
Lower third 1 wall	11 months	Local recurrence and groin glands	Stockholm
Upper and middle thirds 2 walls	11 months	Local recurrence, pelvic and groin glands	,,
Upper and middle thirds 1 wall	5 months	Local recurrence	,,
All thirds 1 wall	22 months	Local recurrence	,,
Upper and middle thirds 3 walls	10 months	Local recurrence and metastases in spine	,,
All thirds 3 walls	9 months	Pelvic gland metastases	Manchester
All thirds 3 walls	6 months	Local recurrence	,,

years in the survival column, as in the previous table, will tell you what has happened to them. The first case in the table was treated 16 years ago, and what radium in the vault was expected to do to a tumour in the lower third, I cannot imagine. In cases 2, 3 and 5 it was hoped that sufficient irridation might reach the middle third, and the others were rather in the nature of palliation.

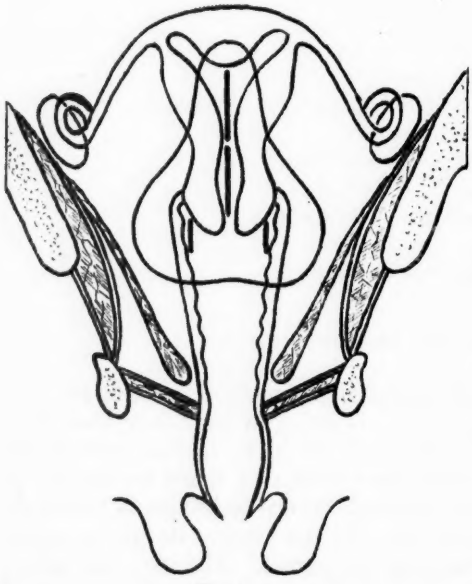

FIG. 2.

A moment ago we considered an arrangement of radium which was adequate for tumours of the cervix. In Fig. 3 I have tipped that curve upside down and by putting the radium source into the vagina instead of the cervix we have an arrangement which is suitable for the intracavitary method of irradiating vaginal tumours. It is, of course, very simple to draw this, but how can this idea be put into action? Several methods have been proposed somewhat on these lines. Clifford White, in 1937, published a method, which he has used. This consists of making a mould of dental stent and putting the radium, usually in the form of tubes, into the periphery so that it lies over the tumour. It certainly holds the radium in position but is liable to certain errors unless closely checked by radiography. Plate II shows a radiograph of a patient whom I treated last year by means of a combined ovoid and stent,

and in that plate you see the radium in the correct position for treating this particular tumour. Plate III shows the first result that I achieved. The distorted arrangement was due to the fact that the stent altered shape when the radium was introduced. In order to fit it into the vagina again it had to be warmed slightly and the pressure of the fingers at its re-introduction was sufficient to produce this effect. The variations of the isodose-curves in these two arrangements are very great.

In 1942 Lederman and Mayneord described an applicator which they developed at the Royal Cancer Hospital with a view to getting accurate apposition of the radium in treating tumours of the lower two-thirds of the vagina. This consists of 2 lead sheets, with a wax centre into which the radium needles are inserted. We ourselves had, as I previously mentioned, tried to solve the problem by placing " ovoids " down the vagina, as the X-ray photograph in Plate IV shows, but I do not consider

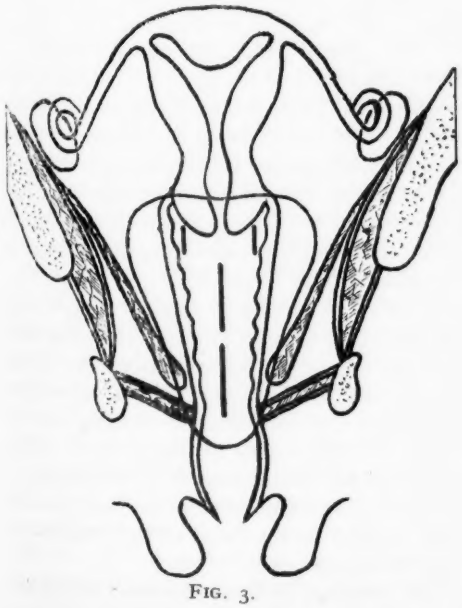

FIG. 3.

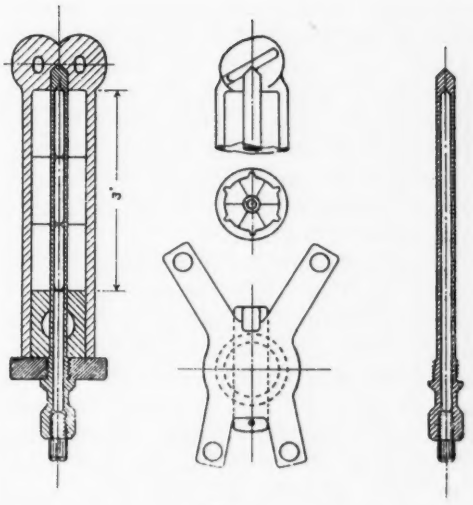

FIG. 4.
Line drawing of the vaginal applicator.

any of these methods free from criticism, largely on the score that accurate apposition of radium is not a certainty and, in the case of the Cancer Hospital applicator, that it is cumbersome, because each case has to have a new applicator designed for it.

What we require is an applicator which will fit as large a number of cases as possible, conform to the arrangement which I have previously suggested, and ensure accurate apposition of radium during the time of treatment.

During the last 12 months my colleagues John Thurgar and Frank Farmer, and I, have devised an applicator which we believe will go far to solve the practical difficulties encountered in obtaining the desired arrangement. Fig. 4 shows a line drawing of this applicator.

*The applicator.** The applicator consists of a hollow vaginal tube to the upper end of which are attached 2 oval-shaped radium

* Physical and constructional data will be published elsewhere at a later date.

containers, similar in design to the "ovoids" used in the Manchester cervical technique. These are arranged to irradiate the parametria and the upper part of the paravaginal tissue. The hollow vaginal portion of the applicator carries, centrally, a metal stem into which can be placed 1, 2, or 3 radium sources according to the site and extent of the tumour.

Screenage is effected by inserting a heavy metal (gold or lead) around the stem, 6 segments forming the complete circle. The object of the screen is to enable high intensity irradiation to be given to the tumour and at the same time to protect the non-involved surrounding tissue. The number of segments of screen inserted will therefore vary in each case, and will depend upon the site and extent of the tumour. The screens are also divided longitudinally into thirds so that it is possible to have every combination from total screenage except for one sixth of the circumference of any given third of the vagina, to no screenage at all.

At the lower end the vaginal tube is closed by a solid cylinder carrying 4 projections (2 anterior and 2 posterior) to which the supporting harness is attached. The straps of the harness are adjustable and fit on to a belt around the patient's waist.

The whole apparatus, with the exception of the metal screens and central radium container, is constructed of a transparent acrylic resin and a material known commercially as "Stellon" has been found most suitable for the purpose. This material allows sterilization by boiling, is light in weight, and its transparency enables inspection of the tumour through its walls, and thus it is possible to plan the arrangement of radium and screens in direct relation to the size and position of the tumour.

The oval-shaped containers, which constitute the head of the apparatus, each carry 18.75 mg. of radium and the container in the stem can accommodate, as a maximum, 3 tubes of 25 mg. each. Here again wide variations of arrangement are possible. Thus in a tumour in the lower third, two 25 mg. sources, one in the middle third and one in the lower third, can be inserted and the upper tube and radium source in the head of the applicator omitted. Similarly in a tumour situated in the upper third, the 25 mg. source in the lower third is not inserted. When it is not desired to insert a lead or gold screen a Stellon blank is inserted in its place and thus the position of every screen is accurately stabilized.

The tumour is inspected with the empty applicator *in situ*, and the arrangement of radium and screens is decided. The applicator is removed and the appropriate screens inserted, and if radium is to be used in the head of the applicator it is placed in position at this time. The applicator is now re-introduced and the harness attachment fitted to the lower end and locked by a clamping pin which prevents rotation during treatment. The vaginal radium sources in the central tube are assembled by a technician and where a 25 mg. tube is not required a brass blank is inserted in its place. This tube is now brought to the theatre loaded, and is inserted and fastened by a screw thread, and in this way all unnecessary exposure of the operator to comparative large amounts of radium is avoided (Plates V and VI).

Plate VII shows a radiograph of our of our applicator *in situ*. This particular tumour was a rather extensive one lying in 3 walls of the vagina in a somewhat corkscrew fashion, thus accounting for the bizarre arrangement of the screens. As it extended the whole length of the vagina 3 sources were employed in the central tube and radium in the head of the instrument can be clearly seen.

We propose in future to use this instru-

ment in such cases of carcinoma of the vagina as we encounter. We hope also that it may prove useful in treating cases of carcinoma of the cervix which have extended a long way down the vagina and we intend to employ it in the pre-operative irradiation of carcinoma of the corpus, since the presence of isolated nodules low in the vagina is not uncommon in this disease. Whilst we were designing this applicator Focht, Marinelli and Twomby (1947) of the Memorial Hospital, New York, published an account of an applicator of somewhat similar design. Their apparatus consists of a perspex cylinder into which fits a lead core with eccentrically placed radium tubes. We believe that the irradiation of the parametria by the introduction of radium into the fornices is an improvement on their design, and that the centrally-placed radium source in our applicator is a superior physical arrangement.

Conclusions.

It would appear from this study that we have tended to reject some cases which, had a little more thought been exercised, would have proved amenable to treatment. Secondly, as far as radiotherapeutic methods are concerned we have not always been careful to irradiate the tumour adequately, and indeed we did not posses an instrument which would allow us to do so with any degree of accuracy; and thirdly, we have seriously neglected the lymphatic drainage of the vagina. There is one other factor which I must mention and that is that we have undoubtedly irradiated a certain number of tumours which were not likely to respond favourably to radium. In the last few years Glucksmann and Spear (1945) have developed a method of determining the response of an individual tumour to irradiation. Briefly, their method consists of estimating the percentage of viable and non-viable cells in a given area of growing tumour edge before irradiation and comparing it with further sections taken during treatment. If there is a great reduction in the percentage of viable cells the prognosis, provided the irradiation is adequate, is considered favourable, but where no such reduction takes place an early reawakening of tumour activity may be expected. This method has been used extensively in cases of carcinoma of the cervix with a high degree of accuracy. It is equally applicable to cases of carcinoma of the vagina, and I now employ it as a routine. Part of the dose of radium can be given as a test without vitiating later surgery if the tumour proves unresponsive.

Provided the tumour is likely to respond to the effects of irradiation, I believe that radium is the method of choice in dealing with vaginal cancer and that if accurate apposition of the radium sources can be achieved many cases which have previously proved fatal may be saved.

Radical surgery as the main line of attack on vaginal cancer in general will never, I think, be the method of choice for most people. The radical operation for carcinoma of the vagina is a formidable undertaking, much more serious than Wertheim's operation for cancer of the cervix, of which it is an extension; but I should not like to think that it will altogether disappear from the gynaecological armoury, because there are undoubtedly some tumours which, although limited, will not respond favourably to radium, and in these cases I believe that radical surgery will play a small but very important part.

As an ancillary to radium, surgery is most valuable. When the groin nodes are likely to be involved the radical block dissection is vastly superior to X-ray therapy, and in the case of the iliac nodes I believe that the iliac adenectomy operation of

Taussig may also prove superior to present methods of deep X-ray therapy. As a means of diverting the urinary or faecal flow surgery has not been employed sufficiently. If we can cure a carcinoma of the vagina only at the expense of stenosing the rectum, then surely colostomy is as justifiable as if we were dealing with a rectal cancer.

In my opinion the stumbling block to progress in the treatment of this disease is not so much a lack of ideas or of methods as our almost complete ignorance of the clinical behaviour of this rare form of cancer. We can, I feel certain, despite this rarity overcome the difficulty, and I should like to see a registry of vaginal tumours set up at which clinical details and pathological findings could be pooled and analyzed for all cases occurring in this country, in the same way as registries for osseous tumours and lymph nodes have been set up at the Royal College of Surgeons, and at Oxford. This college could play a leading role in such a scheme, especially if its Fellows and Members will contribute their information, no matter how small; and if our friends, the radiotherapists, possibly through the offices of the British Institute of Radiology and the Faculty of Radiologists, joined with us in such a scheme I am certain that it would cover almost every case of carcinoma of the vagina occurring in the British Isles. Perhaps if such a registry had been in existence I could have given you, for example, the results of the radium treatment of 270 cases instead of 27.

Some years ago, at a discussion on cancer of the vulva at the Royal Society of Medicine, F. J. Browne (1939) made a plea for the concentration of the treatment of that disease, on account of its comparative rarity, in the hands of a few interested people and by this means he suggested that some at least would gain a wide experience in its treatment. In Newcastle my colleagues have very generously adopted that view and handed me their cases of vulval cancer to treat. The improvement I have effected in my own technique is great and the results are better in consequence. How much more necessary such a concentration of vaginal cancer is, I hope I have made clear to-day.

Clinical material is the basis of clinical research, and in cancer, clinical research at the present moment, if not dead, is very moribund. The focus on cancer research has shifted from the ward and operating theatre to the laboratory, and those of us who are clinicians must take our share of the blame for this. It is up to us to play our part and make our contribution, for, make no mistake, the laboratory worker is as dependent on us as we are on him; the final test is on the man and not on the mouse. By a reawakening of clinical cancer research in gynaecology we shall follow an example set for us by the man to whom our College owes so much, William Blair Bell.

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AETIOLOGY OF ECLAMPSIA

BY

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THE term "toxaemia of pregnancy" was introduced at the end of the 18th century. The hypothetical toxin has been sought in the foetus, in the placenta and in the mother, but the search has been fruitless and no peculiar toxin has been found. Though many effects of morbid metabolism have been found in cases of toxaemia, not one of these has been found to be present in all cases. The only signs which are present in different degrees in nearly all cases are oedema, hypertension and renal damage shown in albuminuria or more gross urinary changes. For 25 years I (1922) have doubted whether these clinical phenomena are caused by a toxin. It seems to me quite possible that all the typical phenomena can be explained by changes in the circulatory system during pregnancy. In a recent publication G. Smith and O. Smith (1947) reported a high level of gonadotrophic hormone to be characteristic of patients with toxaemia, even before the appearance of clinical symptoms. They conclude however, that the primary cause probably lies in a deficiency in the uterine circulation.

After reviewing some general problems in the physiology of circulation I shall discuss first the changes brought about by normal pregnancy and then the changes in what has so far been called toxaemia of pregnancy.

Before discussing the influence of pregnancy on the blood-supply of the uterus and its surroundings, I want first to consider what we know about the distribution of the blood in normal circulation and in this I follow chiefly Hess (1930) and Lovatt Evans (1945).

The total volume of blood is not sufficient to provide all organs with a maximum supply of blood at the same time. The continual fluctuations in activity of various organs call for continual changes in their blood-supply.

The normal circulation of the blood is able to anticipate these changes and regulate them on behalf of those organs which require more blood in periods of increased activity. The ultimate purpose of the circulation is the distribution of blood to the various capillary areas in actively functioning tissues. The reflex coming from an organ to regulate the entry of blood necessary for the time being to feed its tissues is called by Hess the nutrition-reflex. The volume of blood flowing through the various organs shows wide variations, depending chiefly on the intensity of metabolism in the organ and so on its oxygen requirement. During increased activity blood has to be transferred from temporarily inactive organs to active ones. This is regulated chiefly by the central nervous system, but the smaller variations in blood requirement can be regulated reflexly and this reflex grows stronger as the activity of the organ increases. The increased blood-supply is brought about by dilatation of the arteries and arterioles and the afflux in larger capillary areas. Not only does the change in the flow of blood influence the arterial area concerned, but the interplay of collateral and neighbouring areas can

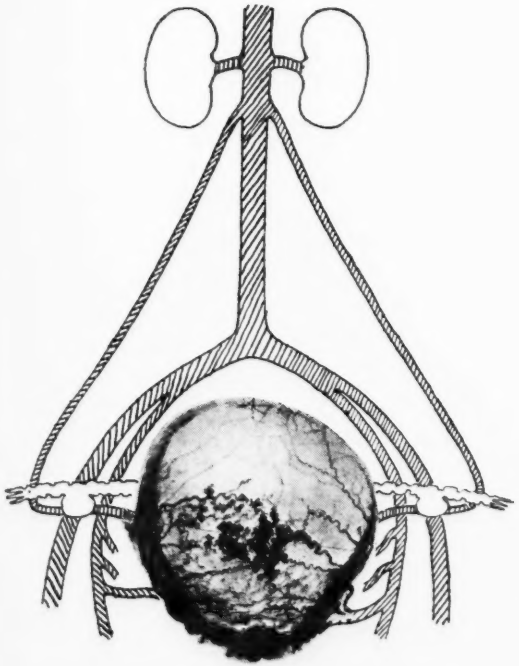


FIG. 1.
Uterus showing the arterial blood-supply to placental site.

FIG. 2.
Sections through the placental site.

FIG. 3.
Further sections through the placental site.

The influence of tonicity and of contraction of the muscle must be very important.

Difference in the blood-supply of the uterus between nullipara and multipara without pregnancy and in the first months of pregnancy.

FIG. 4.
Arterial blood-supply in human uterus. Nullipara. (Horn, 1918).

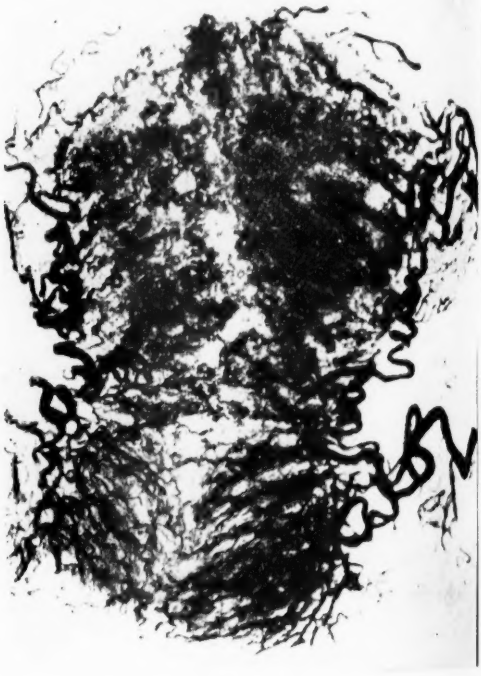


FIG. 5.
Arterial blood-supply in human uterus. Multipara. (Horn).

FIG. 6.
Arterial blood-supply in the uterus of the cow. Nullipara.

FIG. 7.
Arterial blood-supply in the uterus of the cow. Multipara.

FIG. 8.
Arterial blood-supply. Cow, nullipara, 2 months pregnancy.

FIG. 9.
Arterial blood-supply. Cow, multipara, 2 months pregnancy.

Difference between the uterus of multipara and primipara with eclampsia. Arteries and muscle in the uterus of multipara are larger and thicker.

FIG. 10.
Uterus of multipara.

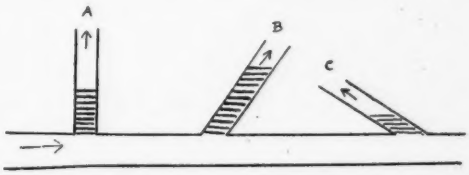
FIG. 11.
Uterus of primipara with eclampsia.

also help to regulate the augmented flow. The increase in the quantity of circulating blood can be supplied by the blood reserve in the spleen, liver and other areas, such as the splanchnic area. If this is not sufficient, blood has to be withheld from other organic areas by means of vasoconstriction of the arteries in these areas. The heart need not necessarily be overburdened if the demands made on it are not too high.

According to Hess the strongest reaction is brought about by the organs that are most important for life. Of first importance is the area of the coronary artery, then the brain and the lungs, which all continually demand a large supply of blood; then come the areas for which requirements are elastic, the muscular area as an ever-ready apparatus for movement, the skin with its heat-regulating function, the renal and hepatic areas and lastly the splanchnic area with the weakest reaction and this only during digestion. There will also be a constriction of the venous vessels to increase the supply of blood to the heart and enlarge the minute /volume output of the heart. The extent of the area and the intensity of the reflex influence the extent to which the relief areas are involved in the reaction.

The direction in which an artery leaves the main artery is also of importance for a sufficient flow of blood through an organ. If the branch inclines at an acute angle to the direction of the flow the end-on pressure in the branch is greater than if the branch were at right angles, in which case the hydrostatic pressure in the branch would be equal to the lateral pressure on the wall of the main vessel (see diagram).

This is of importance in the supply of the kidneys, where the branches are at right angles to the aorta. It is also of importance in the case of the uterus, as the uterine artery enters near the cervix and after that the main branches bend immediately upwards, almost at right angles, although the anastomosis with the ovarian artery makes the circulation easier. A second point which I want to make is the effect on the circulation



A. Situation in the renal artery. The branch is at right-angles, hence the hydrostatic pressure in the branch is equal to the lateral pressure on the walls of the main vessel.

B. Situation in the hypogastric artery. The branch is at an acute angle to the direction of the flow. The pressure will be greater than the lateral pressure in the main stem.

C. The branch of the uterine artery is at an obtuse angle and the pressure will be less than the lateral pressure in the main stem.

when the resistance increases in an organ that is supplied with blood through a side-branch. Here we shall also find a dilatation of the arteries. In this case a sufficient flow of blood can be supplied only by increased pressure in the main artery with the assistance of the general circulation, brought about by an increase of the output of the heart; but the most important point is the vasoconstriction in the peripheral arterioles. The experiments of Goldblatt, and his colleagues (1931, 1934, 1937, 1938, 1940), Wilson and Byrom (1939) are very important for an understanding of the aetiology of hypertension. When a clamp is applied to one of the renal arteries a rise of blood-pressure results, not persistent or affecting the function of the kidney. Slight constriction of both arteries gave rise to mild hypertension. Wilson and Byrom, who carried out their experiments on the rat, found moderate constriction to be followed by hypertension and severe constriction by hypertension with convulsions and marked changes in the blood-vessels. This constric-

tion affects a branch which leaves the aorta at a right angle. The only possible means of compensation to increase the pressure in the renal artery is vasoconstriction in the periphery, increased blood-pressure and increased minute/volume output of the heart. The nutrition-reflex in the kidney is of a chemical nature, a polypeptide, hypertensin, which acts as a pressor substance and causes continual hypertension. On the other hand an increase of blood-pressure from other causes will also cause vasoconstriction of the arteries in the kidneys so as to prevent an overflow. This, too, has been proved by placing the kidney in Shäefer's plethysmograph, whereupon after irritation of the peripheral end of the anterior root of the 10th dorsal nerve an increase in blood-pressure was observed, together with a diminution of the volume of the kidney and active contraction of the arterioles of the kidneys. The general circulation reacts with a rise in blood-pressure if a sufficient number of arterioles are constricted, but not if the vessels are entirely closed. A rise in blood-pressure is found in most people after repeated determinations at short intervals.

Let us now consider the reactions which pregnancy can bring about. During pregnancy alterations in the circulation of the blood will occur under physiological conditions. The uterus and its contents demand an increased supply of blood which must flow in constantly, otherwise the foetus will not be sufficiently supplied with oxygen. Soon after impregnation the uterus becomes larger and softer and hyperaemia points to an increased flow of blood. This nutrition-reflex can hardly be other than hormonal, very likely from the trophoblast. More blood is carried to the uterus and this is made possible by hypertrophic changes in the blood-vessels, the calibre of the arteries being doubled. There is dilatation of the blood-vessels, not only in the uterus but also in its surroundings. It is physiological that the walls of the capillaries become permeable. A larger quantity of blood is available, for an increase of 15 per cent in the total volume of blood has been established. During the first half of pregnancy the growth and hypertrophy of the uterine muscle are more rapid than the growth of the uterine contents. In the first months the uterine wall hypertrophies without any increase of uterine pressure. In the fourth month the thickness is one inch. The muscle is atonic and responds only slightly or not at all to pituitrin. There is no increase in resistance to the circulation of the uterus during the first months of pregnancy. A strong nutrition-reflex is brought about by the growing foetus and placenta, but the inflow of blood is not yet complicated by resistance in the area to which the blood is to be supplied. The venous blood flow is sufficient and free. There is a general increase of fluid in the tissues surrounding the uterus. This slight oedema accompanies the physiological changes of pregnancy and is necessary later on for making birth easier. It is therefore a physiological phenomenon.

In order to fulfil the demands of the nutrition-reflex of the uterus compensatory reactions take place in the general circulation. This can be considered probable, as the reflex acts in an area in the middle of the body, an area of blood-vessels which has to be continually supplied with more than sufficient blood so as not to endanger the life of the foetus. In order to provide enough blood in this central area of blood-vessels the minute/volume output of the heart of the pregnant women increases to one-third more than that of the non-pregnant woman (Frey, 1923). Observations on the nail-bed carried out with the capillary microscope showed that in normal pregnant women stases in the capillary flow occur approximately four times as fre-

quently as in non-pregnant women (Hinselmann, 1924). Barcroft and Stevens (1928) made it clear that the blood from the reserve depots flows into the circulation, for they found the spleen to be contracted during pregnancy. In addition to the increased blood flow through the capillaries there is an increase of the venous pressure not only in the lower part of the body but also in the upper part (Runge 1924).

Increased demands are made on the circulation of the blood in the last months of pregnancy. In the second half of pregnancy the contents grow more rapidly and the wall becomes relatively thinner until at the end of pregnancy the wall is one-fifth to two-fifths of an inch thick. It is evident that the intrauterine pressure is slightly increased. In the first months the muscle is weak and atonic and contractions are few, in the later months the tonicity of the muscle increases, the contractions become more frequent and powerful and the response to pituitrin is more marked. The flow of blood through the uterus is very closely connected with the tonicity of the muscle. In order to gauge the tonicity of the muscle I determined its creatine-content (Beker, 1922, 1926, 1929, 1931, 1934, 1942). For the purpose I examined the uterus bicornis of a pregnant cow, in which the percentage of creatine appeared to increase regularly during pregnancy. At the end of pregnancy it was doubled, in the non-pregnant horn it had increased, but to a much less extent than in the pregnant one. Tonicity of the uterine muscle increases therefore during pregnancy and is dependent on the growing contents. The tunica media of the veins is very closely connected to the muscle and the flow of blood therefore is dependent on the tonicity of the muscle.

The uterine artery, which anastomoses freely with the ovarian artery, distributes blood through about 8 branches, which lie in the muscle and form the arterial meshwork at the placental site. The walls of the arteries become thinner as the inner surface is approached. There exists in the uterus a system of blood-vessels which supplies the muscle with blood and also a system of blood-vessels which supplies the intervillous space. The principal reflex comes from the last-mentioned. The reflex requires a large supply of blood for the intervillous space, but the flow depends on the tonicity of the muscle as the blood-vessels run through this muscle. This is clearly shown in the illustrations (Figs.1–3). In the later months of pregnancy, when the woman stands up, the blood will have to flow partly against gravity.

The reactions of the general circulation are also to be seen most clearly in the later months of pregnancy. It is obvious that the increasing uterine contractions must temporarily increase the resistance offered to the blood flow. After each contraction there must be a freer inflow of blood to maintain a sufficient blood-supply in the intervillous spaces. Delivery will therefore demand the maximum of compensatory reactions on the part of the general circulation because of the increased resistance during labour. Clinically Fellner (1923) proved an increase in cardiac output and in blood-pressure at the beginning of labour. By observation with the capillary microscope in the nail-bed the number of stases was seen to increase in the first phase of labour by 18 per cent, and in the second stage by 28.5 per cent (Hinselmann 1924).

In my opinion these favourable compensatory reactions in the general circulatory system are induced by the regional resistance in the uterus and are required to secure an adequate blood-supply for the foetus during and after uterine contractions. Parturition often pushes the function of the circulatory system to its physiological limits. It is often noted during labour that,

as a reaction to the vasoconstriction in the arteries of the kidneys, the urine contains albumen and even casts. We have seen that for pregnancy and labour to proceed within physiological limits the following conditions must be fulfilled : the arteries of the uterus must hypertrophy adequately and the uterine muscle must remain in a state of tension which does not offer an abnormal resistance to the flow of blood. On the other hand the heart must be capable of enlarging its minute / volume output, the arterioles in the periphery must be capable of undergoing a certain degree of constriction, and the permeability of the capillaries must be increased within physiological limits.

Let us now consider the factors liable to cause complications. The term toxaemia is used, although we do not know of any specific responsible toxin. Many years ago I expressed doubts as to whether such a toxin would ever be found, since all the clinical phenomena typical of ' toxaemia ' can be explained by definite changes in the circulatory system during pregnancy. It might be better to speak of ***hypertonia gravidarum***, using the term eclampsia if the vasoconstriction of the arterioles increases to spasm.

The syndrome may be primary, if an abnormal resistance in the uterine circulation has to be overcome, or secondary, if the resistance in itself is normal, but the response to demands on the general circulation to supply the intervillous space sufficiently with blood is deficient.

Primary hypertonia, an increased resistance in the circulation of the uterus, will give rise to a reaction similar to an increased resistance in the circulation of the kidney. Goldblatt, Wilson and Byrom found that vasoconstriction of the renal arteries resulted in benign hypertension and constriction over a longer period gave rise to malignant hypertension. As the foetus requires its oxygen constantly, the circulatory system of the uterus must be supplied with blood continuously. If the resistance increases, the reaction of the general circulation will be an increase of the minute / volume output of the heart, vasoconstriction of the arterioles in the periphery, a frequently interrupted capillary flow with increasing oedema, general hypertension and, as a reaction to the general hypertension, vasoconstriction in the arterioles of the kidneys and other organs as already discussed in the physiological review.

What can be the origin of the increased resistance ?

In the first place there must be an insufficient hypertrophy of the uterine blood-vessels and muscle. This is to be expected mainly in primigravidae as after having once undergone pregnancy the uterine muscles and vessels remain enlarged. From the illustrations (Figs. 4–9) it may be seen that in multiparae the muscle wall is thicker and the arteries, before as well as during pregnancy, are of a distinctly larger calibre.

A disturbance in the required cardiac function is to be expected if a cardiac lesion, antedating impregnation, already requires an increased minute / volume output to prevent decompensation. This holds good particularly for aortic stenosis and for women of an infantile type. The arterial system of these women is under-developed, a constitutional hypoplasia of the arterial system being responsible for subarterialization of certain organs. An infantile uterus is often the manifestation of subarterialization. The same aberrations are found in women with hormonal deficiencies which give rise to obesity; here also, the uterus may be infantile. The women in whom primary hypertonia and eclampsia occur are those of the young, infantile type and the obese type. Alvarez observed high blood-pressure in young women not yet full-grown.

According to von Zarday (1930), 90 per cent of patients with obesity show objective symptoms of disturbance of the general circulation. Hermann (1929), too, found aortic narrowing in 44 per cent of cases of eclampsia, a fact first noted by Lohlein. After the first pregnancy the uterus remains enlarged, the uterine vessels remain widened and so the uterus is better prepared for a subsequent pregnancy, if no damage has been suffered in the preceding one.

In the second place unfavourable developments are to be expected if the contents of the uterus are growing abnormally quickly. In such case the tonicity of the uterine wall will increase rapidly and the entry of arterial blood to the intervillous spaces, which is dependent on a normal tonus of the uterine wall, will be diminished because hypertonia of the uterine wall will give rise to an increase of the resistance.

This is to be expected in multiple pregnancy, hydramnios, a rapidly growing hydatidiform mole and, to an acute degree, in accidental haemorrhage. In multiple pregnancy, especially in primigravidae, hypertonia and eclampsia occur 5 times as frequently as in single pregnancy. In hydramnios complications are often observed. With hydatidiform mole the symptoms are often hyperemesis and pre-eclampsia. In a series of 30 women with molar pregnancy Page (1939) noted pre-eclamptic complications in 10. There were no complications in 16 before the 4th month. Of 14 between the 4th and 7th months 10 showed serious complications. In these women the contents of the uterus are growing rapidly and as the nutrition-reflex is stimulated most probably by the chorion, the demand for blood will be stimulated and will be abnormally intense, as long as the mole is active. In the beginning there will exist only a strong reflex, after the 4th month the increased resistance will become of importance. The symptoms of pre-eclampsia will be superimposed upon the symptoms of hyperemesis. If the mole stops growing the complications decrease although the mole is not expelled.

Separation of a normally implanted placenta has its special place in pathology. As I have shown, accidental haemorrhage results from the rupture of an arterial vessel between the muscle wall and the placenta, where the arteries have a very thin coat. Without doubt nephritis and hypertension are predisposing factors, but as Young (1927) and Paramore (1928) have shown, there are patients without such lesions who develop accidental haemorrhage. I have treated women in whom the cause was an injury or other acute increase in the circulation of the uterus. Such cases are most important in showing the influence of a sudden increase of resistance in the uterine circulation. A retroplacental clot is formed, which in concealed cases will cause a sudden increase of tonicity of the uterine wall and a sudden increase of resistance in the uterine circulation. At the moment of rupture of the artery the muscle is not contracted and the blood will be squeezed between the lamellae of the muscle. Albeck (1920) found albuminuria in 67 per cent of his patients with concealed haemorrhage and in 40 per cent with revealed haemorrhage. The greatest resistance is to be expected in totally concealed haemorrhage. As far as I know cortical necrosis of the kidneys is found only in the concealed, never in the revealed variety. In the latter there is no severe resistance.

Secondary hypertonia. The resistance in the pregnant uterus is normal but the peripheral circulation is incapable of responding to this normal resistance and the nutrition-reflex which demands a sufficient blood-supply for the placenta. The consequent

failure might arise from the low reserves of the general circulation, or from hypertension existing before pregnancy, or from disease of the peripheral vessels due to nephritis. There will not be a sufficient reserve present to compensate for the extra strain involved in overcoming the resistance in the side-branches of the circulatory system.

It is possible that the low reserve of the circulation may not have been noticed before pregnancy or that essential hypertension or nephritis may have pre-existed. A low-reserve circulation may be due to hypertonia or to eclampsia in a previous pregnancy. It will depend on the reserve of the general circulation whether failure will occur or not. Multiparae especially may go through pregnancy without difficulties provided that the extra demands for the circulation in the uterus are not too high. In the first 5 months signs of failure are not common, for they mostly occur in the later months of pregnancy, as is to be expected after my explanations.

Gibberd (1931) made it clear that 50 per cent of patients with primary hypertonia had renewed hypertonia in the next pregnancy, mainly when the disease had lasted longer than 3 weeks, although they had been without symptoms in the interval. He calls this "occult nephritis". Stander (1929) speaks of low-reserve kidney. I should call this low-reserve circulation. Browne (1937) classifies all these cases as pre-eclamptic toxaemia. Although many such patients develop hypertension or nephritis after many years, there are also women who remain without symptoms when they are not pregnant. More complications are to be expected in essential hypertension, where the reserve is in most cases lower than normal. We know that essential hypertension in itself may be mild or severe. We may speak of essential hypertension in primigravidae only, as in multigravidae the hypertension may be the result of the preceding pregnancy. I have an impression that the prognosis in essential hypertension is more favourable than in hypertension from low reserve after a previous pregnancy. If the hypertension has existed for a longer period and the vessels are sclerotic, the influence of pregnancy is always serious. Although some cases are described in which nephritis has been favourably influenced by pregnancy, this is exceptional. It is possible that the reactions of the general circulation to the pregnancy may be stronger than the demands of the uterine circulation. The mildest degree of nephritis may be considered to be a low reserve of the circulation. If the woman is not pregnant not all of the glomeruli are in function at the same time, during pregnancy the reserve may be too low. Chronic nephritis, and especially interstitial nephritis, is usually adversely influenced by pregnancy. We have shown that, especially in the later months of pregnancy, the arterioles of the periphery and also of the kidneys must constrict to compensate for the reactions in the circulatory system required to secure an adequate blood-supply to the uterus and its contents. Sclerotic vessels are unable to contract further and the arteries of the uterus will also be sclerotic and unable to dilate sufficiently. The effect will be an insufficient supply of blood to the intervillous spaces and the formation of infarcts. Infarcts are not always due to haemorrhage. Their formation may be due to a gradual interruption of the circulation of the intervillous spaces. The placenta is in many cases abnormally small. The foetus will not grow and will die in the early months. Death of the foetus can better be accounted for by deficient circulation in the intervillous spaces than by some unknown toxin. If the arterioles are still able to contract but the reaction is generally insufficient, the renal disease increases, the blood-pressure

rises, the foetus remains small and, in the later months, when the circulation in the intervillous spaces is insufficient, the foetus is born prematurely or dies *in utero*, the mother's nephritis meantime becoming worse. The exacerbation of the nephritis is expressed by increasing oedema, generally not as marked as in primary hypertonia. The blood-pressure is high and does not fluctuate, albuminuria is marked and the urine also contains blood-cells and casts.

Anaemia points to secondary hypertonia as do also sclerotic changes in the retina and a high blood-urea. Eclampsia results in secondary hypertonia earlier in pregnancy than in primary hypertonia. Eclampsia without convulsions is nearly always due to secondary hypertonia.

I shall now discuss some clinical facts, which are in favour of my theory and against the theory of 'toxaemia'.

The illustrations (Figs. 10, 11) show that the uterus of the eclamptic patient is much thinner and the arteries are smaller than in multiparous uterus.

The following table compares the size and weight of 5 uteri, acquired by operation or necropsy.

	Weight in g.	Circumference in cm.	Length in cm.	Width in cm.	
1. Primigravida (8 months)	1200	43	24	18	with placenta.
2. Eclamptic primigravida	950	33	19	18	with placenta.
3. Multipara (9 months)	1650	—	—	—	without placenta.
4. Multipara (3 days postpartum)	1300	40	21	16	without placenta.
5. Eclamptic primipara (3 hours postpartum)	1100	35	19	15	without placenta.

Both with and without placentae the uteri of eclamptic patients are smaller and lighter than normal. The uterus is in many cases smaller than usual for the time of pregnancy. The children are often under weight. Dieckmann (1938) found 11 per cent under 2000 g. and 44 per cent under 3000 g. Infarcts are rarely seen in primary hypertonia, where the vessels are constricted but not sclerotic. In secondary hypertonia with sclerotic vessels infarcts are much more frequent. The hypertension of the arterioles is observed on examination of the fundus oculi. Narrowing of the vessels with and without oedema was found by Wagener (1933, 1934) and Mylius (1928) in nearly all cases with a blood-pressure above 150 systolic and 100 diastolic. In primary hypertonia retinitis with sclerotic changes is very rare but sclerotic changes are to be expected in secondary hypertonia.

A strong argument against 'toxaemia' and for a disturbance in the circulation is death of the foetus. If the foetus dies *in utero* the general condition of the mother usually improves. The contents of the uterus diminish, the tonicity of the uterine wall decreases too, and the resistance is lower.

The hormonal reflex, which starts in the placenta and demands an uninterrupted circulation of blood in the uterus, will decrease slowly because the placenta will not die at once. A weakened reflex will continue as long as the placenta is functioning. During labour the resistance increases temporarily and in many cases a temporary rise of albuminuria and blood-pressure can be observed during parturition even in cases when the foetus has been dead for a long time. Powilewicz and Morace (1924) followed the progress of 94 patients. In 23

the condition became normal after the death of the foetus, in 5 albuminuria was found again during labour. In 71 the albuminuria persisted and in 8 cases exacerbation was found during the second stage, owing to the more powerful contractions.

Intercurrent eclampsia is in my opinion not to be explained as a toxaemia, especially when the foetus survives. I cannot believe that with conservative treatment, such as rest, narcotics, possibly venesection, a toxin can be removed or a hormonal disturbance cured. Only the circulatory system is influenced by our therapeutic measures, rest in bed being the most important factor, making it easier to augment the flow of blood to the fundus uteri, if the patient is lying flat. Rest in bed without any other therapy leads to decrease of oedema (Wesselink, 1931).

The effect on renal function is caused by vasoconstriction in the renal circulation. Wesselink ascertained that when the intake of fluid was stable, the albuminuria could show variations of 2–20 per cent. It should also be mentioned that both kidneys are not affected to the same degree (Peters, 1922). Narcotics decrease the spasm of the vessels. Venesection does not influence the arterial pressure unless a very large quantity of blood is removed, but a moderate venesection of 300–400 ml. has a remarkable influence on the venous pressure, which lasts many hours (Eyster, 1929). In postpartum eclampsia the uterus usually contracts promptly and the actual loss of blood is often reduced to below normal. Thus the total quantity of blood retained within the circulatory system remains relatively large and this fact in itself is liable to interfere with a speedy return to normal conditions. The arterial pressure will in many cases fall only to rise again later. Probably the process of restoration is dependent on the extent and degree of pathological changes in the tissues and on whether regeneration is possible quickly or at all. I believe that all the pathological-anatomical changes are to be explained by spasms of the arterioles. Braunmühl (1928) has shown that all pathological lesions in the brain are the result of spastic ischaemia. Fahr (1924) observed the same changes in the livers of dogs dying after poisoning with adrenaline. The haemorrhages in the liver are to be found especially on the surface, where the arterioles of the hepatic artery pass into the capillary system, and where the vasoconstriction will be more distinct than in the area of the portal vein. Cerebral haemorrhage and pulmonary oedema are in most cases the causes of death.

If these opinions are correct, experiments on animals can never give a true picture of human eclampsia. The human uterus is one connected muscle which surrounds the contents as a whole, its contractions being aperistaltic (de Snoo, 1946). The resistance in this area is uniform, thus differing from the peristaltic uterus of most animals. Even if labour contractions set in, a peristaltic uterus will never give such resistance to the blood flow as does a contraction in an aperistaltic uterus. The erect position of the human body interferes with the uterine circulation as the largest amount of blood enters the uterus by the uterine arteries and has to be brought to the intervillous spaces against gravity.

Conclusions.

The aetiology of eclampsia is to be sought in a disturbance of haemodynamic equilibrium in the general circulation. Normal pregnancy and labour cause a slight vasoconstriction in the periphery and an increased minute/output of the heart. At all times the nutrition-reflex of the pregnant uterus will urgently require a sufficient blood-supply to the intervillous spaces to guarantee the life of the foetus. The reflex is most probably hormonal.

Two forms of the disease should be recognized. The one is due to an abnormal resistance offered to the circulation of blood within the uterine wall, and the other is the result of a deficient adaptation of the general circulation to the requirements of the uterus in pregnancy and delivery. All clinical observations may be explained by circulatory deficiency in spite of a maximal attempt to respond to the nutrition-reflex of the pregnant uterus. The strongest arguments against 'toxaemia' are cases of intercurrent eclampsia and the exacerbation of clinical symptoms during labour long after the death of the foetus.

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OBSTRUCTED LABOUR DUE TO SEPTATE VAGINA

BY

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IT is generally accepted that the presence of a longitudinal septum within the vagina is no barrier to normal delivery, and, indeed, the standard teaching is that in most cases one half of the vagina dilates during the 2nd stage of labour to accommodate the foetus whilst the other half becomes obliterated. It is recognized that occasional difficulty may arise, but the mechanism of such dystocia is not stressed nor are the results of failure to recognize obstruction due to a septum sufficiently emphasized in the majority of textbooks.

A vaginal septum may indicate the presence of deformity at a higher level in the genital tract and is often associated with a double uterus and cervix, but it may equally well exist as the sole deformity, and may then vary from a thin, narrow "string", which gives way before the advance of the presenting part, to a thick, fleshy partition extending between $\frac{2}{3}$ and $\frac{3}{4}$ the length of the vagina. In either variety the diagnosis of its presence should lead to increased care in the management of the labour.

Most of the recorded cases have been of septate vagina associated with uterus didelphys and they have been recorded because some coincidental disturbance of function or anatomy has precluded vaginal delivery. It was, therefore, thought worth while to record the following 2 cases as illustrative of the dangers attendant on vaginal delivery in such a condition and because they illustrate that the danger is present in both types of defect, the vaginal septum alone and the vaginal septum associated with double cervix and uterus.

CASE 1. The patient, a primipara of 26 years, was admitted as an emergency with a breech presentation in advanced labour. No other diagnosis had been made and the patient had not been seen by a doctor though one had been called by the midwife in charge of the case.

The history was of intermittent antenatal care by occasional visits to the local clinic or midwife but the patient had not been examined within the last month or two. She was very vague about her dates but was considered to be due a month hence.

Spontaneous premature labour had commenced 10 hours before admission and had proceeded normally until the midwife was called; she, recognizing that the case was a primiparous breech, notified the doctor, who ordered the patient into hospital straight away. The patient gave no relevant past history except that she had had swelling of the ankles for 2 or 3 weeks.

On examination she was a florid, well-built woman, having strong uterine contractions, 1 every 3 minutes, and bearing down heavily with each pain. Temperature 99°F., pulse-rate 88, blood-pressure 158/100. Examination of her heart and lungs showed no abnormality and abdominal palpation revealed a uterus the size of 36 weeks' gestation, and a breech presentation, with the presenting part deep in the pelvis. There was gross oedema of the face, hands, feet and legs, and the urine showed a heavy albuminuria.

A vaginal examination was made and she was found to have a double vagina: there was an

antero-posterior septum dividing the introitus and extending upwards for 2/3 the length of the vagina. This septum ended above in a sharp, tightly stretched crescentic edge, over which it was just possible to hook the fingers. Further examination, aided by the use of a speculum, showed that the presenting breech was sitting astride the upper edge of the septum, lying as a complete sacro-posterior having 1 buttock and flexed leg at the top of each half of the vagina. The foetal perineum was thus being thrust down on the taut crescentic fold with each uterine contraction.

Under general anaesthesia division of the septum was performed by clamping, cutting, transfixing and ligating in 3 "bites": this technique was necessary owing to the thickness and fleshiness of the membrane, and particular care was taken to protect the foetal perineum from injury. When this was completed full dilatation of the cervix was confirmed and a breech extraction of a living female child, weighing 4 pounds 3 ounces, was performed. An episiotomy had been done to diminish the risk of trauma to the premature foetal skull and by the time this was sutured the placenta had separated and was expelled. Examination of the vagina at this stage showed that the pedicles of the septum had already shrunk down till they were almost flush with the anterior and posterior vaginal walls and bimanual examination of the retracted uterus revealed no evidence of failure of fusion in the Müllerian system. The mother made an uninterrupted recovery, and 9th day examination showed no abnormality remaining in the genital tract, the tags of the membrane having almost disappeared.

During the puerperium, when the gross oedema began to subside, it was noted that her right hand was obviously larger than the left, and she volunteered that her right foot always required a larger shoe than the left foot; this led to a more complete physical examination which revealed a marked hypertrophy of the right foot and leg, right hand and arm, and right breast, with an equally marked hypertrophy of the left (opposite) side of her face. In addition, there was webbing of the 2nd and 3rd toes of the right foot and both feet showed a severe degree of pes planus. There were no signs of pituitary or other endocrine dysfunction and she was discharged on the 10th day with lactation fully established: blood-pressure 135/100, and urine free of albumen. On examination before discharge and again at the postnatal unit there was no clinical evidence of double cervix or uterus: the patient refused to submit to lipiodal hysterogram and there is, therefore, no final proof that the lack of fusion was confined to the vagina though all the clinical findings supported this. No abnormality of the renal tract was found on intravenous pyelography.

The baby was premature and showed signs of asphyxia pallida. It was not, therefore, fully examined at birth but was immediately treated for shock. It responded well and next day was found to have, in addition to bruising of the buttocks, a second degree laceration of the perineum. It was considered, by this time, to be potentially infected, and was therefore treated first with penicillin cream and then by half-strength Eusol packs. The latter treatment so successfully cleaned the laceration that secondary suture was attempted, but the stitches cut out so quickly that further efforts at repair were abandoned and it was allowed to heal by granulation. On discharge, the baby was gaining weight, was fully breast fed, and its perineum appeared to be healing well.

CASE 2. This patient, also a primipara, had somewhat sketchy antenatal care and stated that during the course of this she was never examined vaginally. Her expected date of delivery was at the end of May 1938, and on April 10th of that year she went into premature labour. So far as she knows she was well during the pregnancy and the premature labour was spontaneous in onset and not associated with any trauma or pathological condition. The labour began at 9 p.m. and she states that she was delivered with chloroform and instruments of a living male child, weighing over 2 pounds, at 1 p.m. the following day. Since then she had had continual incontinence of urine though now, after 10 years, she has periods of dryness. Very little additional history of the delivery was obtained from the doctor and midwife in attendance. They recollected that there had been delay in the descent of the head, that forceps had been applied and that although the infant was small the delivery had been difficult.

Fourteen weeks later the patient was sent in to hospital, where a vesicovaginal fistula was found through which it was possible to pass 2 fingers into the bladder. There were also the remains of

a longitudinal vaginal septum on the anterior and posterior vaginal walls and these were continued across the vault of the vagina as a complete membrane dividing the upper third of the vagina into two. A small but normal cervix was present in each half, and lipiodol injection revealed a complete double uterus. The sequence of events appears to have been that during labour the descending vertex, presumably by pressure necrosis, had broken through the middle of the vaginal septum, thereby coming to lie on one side of the lower third of the membranes while the trunk and limbs remained on the original side. The efforts at delivery had then succeeded in tearing away this portion of the membrane and with it part of the neck of the bladder and the posterior wall of the urethra. In view of the extent of the fistula, repair was regarded as impracticable.

On examination recently, the vulva and urethral orifice looked normal, but as soon as a speculum was introduced and the posterior vaginal wall retracted, a gush of urine followed, and it was observed that the whole of the posterior urethral wall was deficient. The injury appeared to have involved the internal sphincter of the bladder also, for there was no evidence of control other than the somewhat uncertain one of the sphincter vaginae. The vaginal walls showed both anterior and posterior longitudinal ridges which passed upwards to end in a short membrane dividing the upper fourth of the vagina into two, each half containing a normal cervix. Owing to the thickness of the abdominal wall satisfactory demonstration of the double uterus was not obtained, and in view of the X-ray evidence for its existence, obtained during her previous stay in hospital, further investigation was not considered necessary. She was in good health and had not had any other pregnancies. Repair of the defect by Bonney's flap method is under consideration.

In commenting on these 2 cases the first important point is the absence of antepartum diagnosis in both, and it underlines the necessity for more adequate antenatal care, including the necessity of careful vaginal examinations at some stage in the antenatal period. The second point is that, as these 2 cases show, if a vaginal septum is found to be present, it is of great importance to estimate its completeness and to establish the presence or absence of uterine maformations. If the septum is incomplete, as it was in Case 1, then there seems to be no doubt that it should be divided before labour begins, for the likelihood of obstructed labour when the presenting part enters the vagina, be it vertex or breech, is high. If it is complete and associated with double uterus and cervix, as it was in Case 2, then although a normal vaginal delivery is probable yet a watch must be kept lest the descending foetus should rupture the membrane centrally and carry away the lower part, with either its anterior or posterior attachments: or become obstructed and be the subject of an operative delivery before the real mechanism of the obstruction is appreciated. Another such case was recorded by Keevil (1943) in which the lower end of the septum was carried away during a normal delivery and with it its attachment to the posterior vaginal wall and perineum. Strean and Portnuff (1948) also recorded a case in which the rupture of the dividing membrane occurred above the level of the cervix, giving rise to a similar type of obstructed labour.

The presence of a crossed hemi-hypertrophy or gigantism in Case 1 is of interest, though I have been unable to find any reference to its occurrence in association with congenital malformations of the genital tract: the patient was quite aware of its existence, was quite philosophical about it, and stated with complete certainty that it had always been present. In view of this assertion, together with the absence of any signs of pituitary or other endocrine disorder and the presence of the webbed toes, it seems reasonable to class this case with the asymetrical congenital gigantisms of unknown aetiology rather than the atypical acromegalics. There was no family history of gigantism.

SUMMARY.

Two cases of obstructed labour due to septate vagina are recorded and the mechanism of the obstruction in each case is described: it is pointed out that this condition may occur without any other developmental abnormality of the genital tract, although it is often associated with uterus didelphys.

The necessity of extra care in the conduct of labour in cases of septate vagina is stressed because of the increased risk of dystocia.

The presence of a crossed hemi-hypertrophy in one of the cases is noted and its aetiology is stated to be unknown.

My thanks are due to Professor E. Farquhar Murray and Mr. H. Harvey Evers for permission to publish these cases.

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A NEW CONTRAST MEDIUM (RAYOPAKE) FOR HYSTEROSALPINGOGRAPHY

BY

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RINDFLEISCH, in 1910, was the first to attempt radiography of the uterus by injecting a bismuth emulsion. According to Douay, in his report before the Fifth Congress of the Association of Obstetricians and Gynaecologists at Lyons, September 1927, Lelorier was the first to inject an isotonic non-irritant fluid into the uterus with the object of determining tubal patency. His results were to have been presented before the Congress at Lille in 1912, but were never published. The use of Collargol for this purpose was described by Cary (1914), Rubin (1914), and Dartigues and Dimier (1916). This was followed shortly by halogen salts, used by Rubin (1920), and by Kennedy (1922). These, in turn, were completely replaced by the iodized oil, Lipiodol, introduced into surgery by Sicard and Forestier in 1922 and into gynaecology by Heuser (1925) and Forsdike (1925). This substance proved to be superior in many ways to previously-used radiopaque substances and soon became very popular, particularly for diagnostic tests of tubal patency in cases of sterility. Later, other iodized oils such as Iodopine, Lipiodine, Pantopaque and Neohydriol were introduced. Good results and excellent opacity were obtained with these oils for several years, but reports from many investigators began to accumulate, describing objectionable features and undesirable sequelae.

A review of these untoward results following the injection of iodized oils into the uterus shows that in general they are due to the retention of the oil and to its slow rate of absorption. Even in the absence of infection, the oil thus retained acts as a chemical irritant and induces the formation of pelvic adhesions. A more pernicious effect on the reproductive organs is the retention of the oil within the Fallopian tube, where it may set up a foreign-body reaction which obliterates the lumen. The more serious complications such as pyosalpinx, pelvic abscess and peritonitis are also in large measure due to local retention and irritation, superimposed on latent infection (Rubin, 1947). These hazards had earlier led Rubin (1936) to conclude that, until a radiopaque substance should be available having the proper viscosity and density to demonstrate permeable tubal strictures and that degree of resorption which would leave no residue within the tubal lumen after a few hours, one would do well in cases of sterility to stop using lipiodol and oils chemically similar to it. More recently Titus (1947) has drawn attention to accumulating reports of oil-embolism, sometimes fatal, following the use of lipiodol, and states that the position is serious because the purposes served never justify the risk. He concludes that iodized oil should not be used in hysterosalpingography.

In attempts to find the ideal opaque substance several preparations have been used. The crystalline iodine compounds uroselectan (Swick, 1929), Diodrast

(Rubin, 1939) and Hippuran (Rubin, 1939) were found to escape too rapidly into the peritoneal cavity, being insufficiently viscous. It then became apparent that something would need to be added to an aqueous solution to increase its viscosity without retarding its absorbability. Neustaedter and co-workers (1933) added a quantity of 50 per cent glucose solution. Titus and co-workers (1937) developed Skiodan-acacia, a solution containing 40 per cent of monoiodomethane sulphonate of sodium (Skiodan) in acacia 20 per cent. Several favourable reports on this substance have appeared but it has not given completely satisfactory results because of inadequate viscosity, and does not seem to have been widely employed. As a result of further research since 1938, Rubin (1941) introduced visco-rayopake for clinical trial. This is a combination of a crystalloid iodine solution* with polyvinyl alcohol. It is soluble in water, is non-toxic, and does not gel or crystallize at room temperatures. Its viscosity (due to its $3\frac{1}{2}$ per cent concentration of polyvinyl alcohol) has been shown (Rubin, 1941) to be fifty times that of skiodan with acacia and more than twice that of lipiodol. Rubin reported the use of this preparation in 81 patients and stated that the opacity was equal to that of the iodized oils, that the contrast medium remained in the Fallopian tubes long enough to permit radiographs to be made and that it was nevertheless almost completely absorbed after 30 minutes with very little evidence of local chemical irritation. He concluded: "It shares all the advantages of lipiodol and other iodized oils but appears so far to have none of their disadvantages." Since the publication of Rubin's paper, Goldberger (1943) has reported the use of visco-rayopake in 72 patients, including 7 cases of sterility; Bernstein (1944) in 52 patients, including 38 cases of sterility; Norment (1945) in 20 patients; and Montgomery and Lang (1946) in 79 patients. All these authors share Rubin's enthusiasm for this new contrast medium.

In 1942, Kjellberg described a method of pelvigraphy in which 20 to 30 ml. of a water-soluble contrast medium were introduced through the uterus and Fallopian tubes for the purpose of visualizing, as negative shadows, the generative organs and other soft-tissue structures. Jefferiss and Samuel (1946), repeating this procedure, tried different water-soluble iodine preparations, pyelosil, perabrodil, etc., and found, in 18 cases, that any preparation used for intravenous pyelography gave equally satisfactory results. They concluded that the method was superior to the conventional one in determining tubal patency.

Personal Investigations.†

It was considered, at the outset, that something more than mere repetition of the work of the first testers of rayopake should be attempted. It was felt that the claims made for its radiopacity, viscosity and absorbability required further evaluation. It was therefore decided to conduct the following experiments, in addition to a

*70 per cent solution of diethanolamine salt of 2, 4-dioxo-3-iodo-6-methyl tetrahydropyridine acetic acid.

†In December 1946, in New York, I received a supply of this preparation, still in the experimental stage, from Dr. I. C. Rubin for clinical trials at the Royal Samaritan Hospital for Women, Glasgow. Subsequent supplies were received through the courtesy of Dr. E. L. Sevringhaus, of Hoffmann-La Roche, Inc., Nutley 10, New Jersey. In a letter dated 8th August, 1947, Dr. Sevringhaus stated that the new opaque medium would be marketed as "Rayopake" and that the iodine-containing compound is now 50 per cent solution instead of 70 per cent as originally described. Unfortunately, Rayopake is not likely to be available in Britain for many months.

series of the usual tubal-patency tests in sterility cases:

1. To deposit equal quantities of rayopake and an iodized oil (Iodatol) on either side of the pelvis in the course of pelvic operations, immediately prior to closing the abdominal wound.

2. To repeat this experiment, enclosing the preparations in slowly-absorbed gauze (Oxycel).

3. To compare the radiopacities *in vitro* by taking radiographs of equal volumes in identical containers.

4. To compare and contrast the relative viscosities of rayopake, iodatol and water at both room and body temperatures.

5. To compare the relative viscosities and radiopacities of rayopake and a water-soluble iodine preparation, used for intravenous pyelography (Pyelosil 35).

It was found that rayopake was rapidly absorbed from the pelvic cavity (Figs. 1 to 6). This confirmed the findings in hysterosalpingography that, usually, there was no trace of rayopake 40 minutes after its introduction, whereas iodized oil was often present weeks and even months later. It was also learned that, while the radiopacity of rayopake is quite satisfactory (Figs. 1 to 7), the shadow is not as dense as that of iodized oil (Fig. 8). The results of viscosity tests are shown in the following table.

Viscosities.

	Relative flow-time	Relative density	Relative viscosity
Results at 15° C.			
Water	1	1	1
Rayopake ...	65	1.23	81
Iodatol	762	1.35	1025
Results at 37° C.			
Water	1	1	1
Rayopake ...	38	1.23	46
Iodatol	254	1.34	338

It is apparent that the viscosity of iodatol at body temperature is more than 7 times that of rayopake. The viscosity of lipiodol (heavy variety) was found, in subsequent experiments, to be similar to that of iodatol.

It was also found that the viscosity of rayopake was 23 times that of pyelosil: their radiopacities were almost identical.

Summary and Conclusions.

1. A brief history of hysterosalpingography is presented.

2. Rayopake (50 per cent solution of diethanolamine salt of 2, 4-dioxo-3-iodo-6-methyl tetrahydropyridine acetic acid with 3½ per cent polyvinyl alcohol), introduced by Rubin in 1941, but new to Europe, has been used in experimental and clinical trials in 50 patients, with satisfactory results and no ill effects.

3. This solution is less viscous and less radiopaque than the iodized oils commonly used in Europe, namely, iodatol, and "heavy" lipiodol, but the viscosity and radiopacity are adequate. The apparent discrepancy in the results obtained by Rubin and myself, in comparative viscosity experiments with lipiodol and rayopake, appears to be due to the fact that we used different types of iodized oil. Rubin used American-made lipiodol, which appears to correspond to lipiodol (Lafay) "F" Fluide, which is much less viscous than the "heavy" variety.

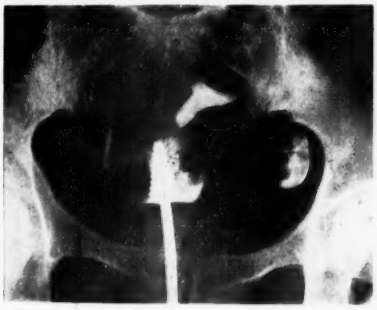
4. The rapid absorption and the fact that it does not possess the undesirable properties of iodized oil are its most advantageous features. Its rapid absorption necessitates exposure of the first X-ray plate within a few minutes after injection.

5. It is agreed, with Rubin, that rayopake is probably the closest approach to the ideal radiopaque medium, yet introduced, for hysterosalpingography. Preparations

FIG. 1

Hysterosalpingogram (Rayopake).

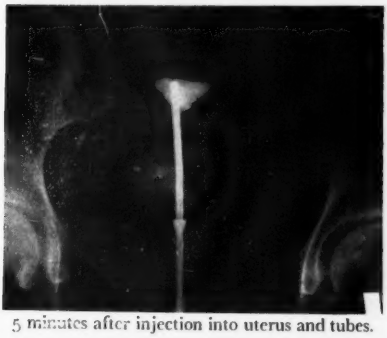
The uterus is well filled and the tubes patent.



X-ray photograph taken 24 hours later showed no Rayopake.

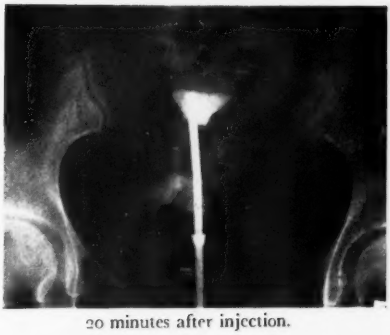
FIG. 2

Hysterosalpingogram (Rayopake).



5 minutes after injection into uterus and tubes.

12½ minutes after injection.



20 minutes after injection.

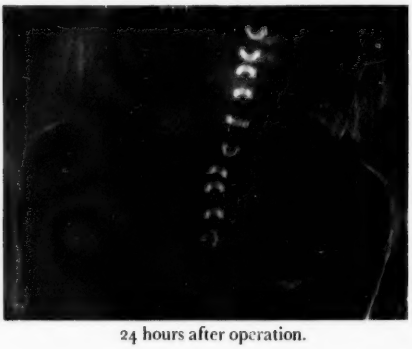
16 hours after injection.

FIG. 3

Rayopake deposited on right side of pelvis, and Iodatol on left side, at completion of pelvic operation.

The clear areas in a vertical row, mid-line, in Figs. 3–6, are due to Michel clips in the abdominal wound.

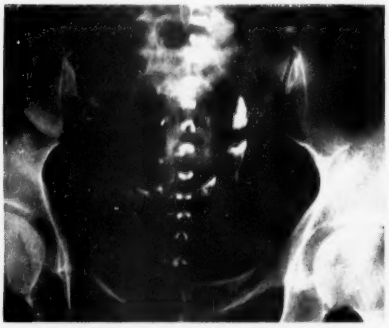
Immediately after operation.



24 hours after operation.

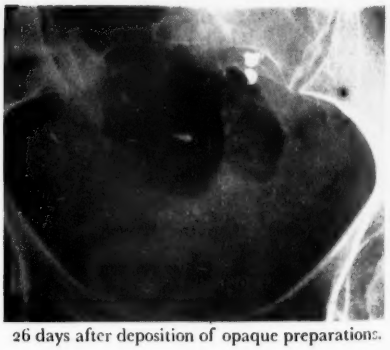
FIG. 4

Rayopake deposited on right side of pelvis, and Iodatol on left side, at completion of pelvic operation.



30 minutes after deposition of opaque preparations.

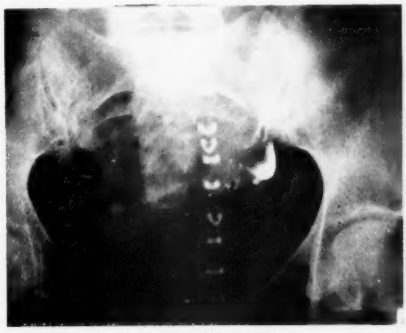
4 hours after deposition of opaque preparations.



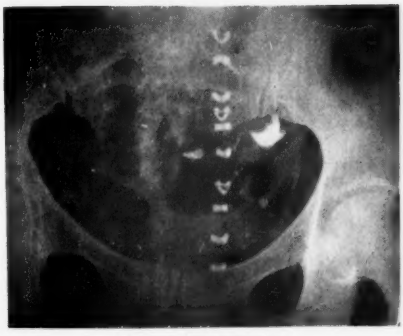
26 days after deposition of opaque preparations.

FIG. 5

Rayopake deposited on right side of pelvis, and Iodatol on left side, at completion of pelvic operation.



At conclusion of operation.

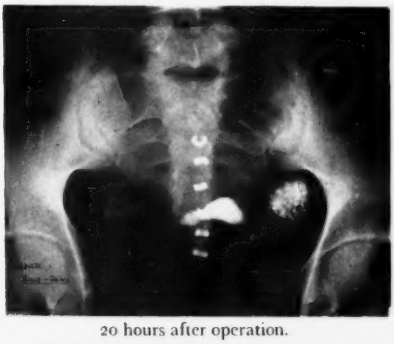


5 hours after operation.

48 hours after operation.

FIG. 6

Rayopake deposited on right side of pelvis, and Iodatol on left side, at completion of pelvic operation. (Each contained within Oxycel gauze.)



20 hours after operation.

48 hours after operation.

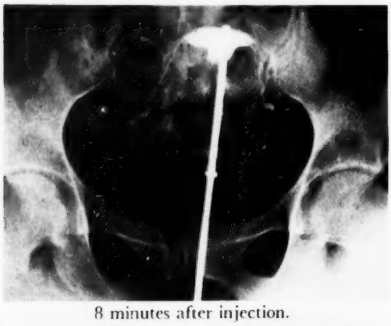
2 weeks after operation.

44 days after operation. Note iodized oil still present.

FIG. 7

Tubal occlusion. Rayopake has not appeared through fimbriated ends.

(Three previous tubal insufflations had shown non-patency at 250 mm. Hg.)



8 minutes after injection.

20 minutes after injection.

FIG. 8

Groups of identical quantities of Rayopake (right) and Iodatol (left) in different types of containers to show comparative radiopacities.

used for intravenous pyelography are insufficiently viscous.

6. With the advent of a non-toxic, rapidly absorbed dye such as rayopake, hysterography or hysterosalpingography can become readily adaptable to routine use.

7. It is agreed that, when supplies of this new medium become available, there should be no longer any place for an oily contrast medium for hysterosalpingography.

I am indebted to Dr. Donald McIntyre for clinical facilities and to Dr. R. Wright, Physical Chemistry Department, University of Glasgow, for the viscosity results.

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RHESUS FACTOR ISO-IMMUNIZATION AND HAEMOLYTIC DISEASE OF THE NEWBORN*

BY

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MUCH general interest has been manifest in the rhesus factor since the original report was published by Lansteiner and Wiener (1940). The obstetrician should be concerned in particular with this subject because certain complications which occur in obstetric patients are directly associated with incompatibilities of the rhesus blood-groups.

The rhesus factor is an antigen which is present in most individuals of the white population. This antigen is found chiefly on the surface and in the stroma of erythrocytes. The original work showed that sera obtained from rabbits previously immunized by injections of rhesus-monkey red-blood cells had a selective agglutinating action on the red-blood cells of various human individuals. This rabbit anti-rhesus serum agglutinated the red-blood cells in 85 per cent of a large series of cases taken from the white population. This reaction was independent of the A, B, and O blood groups, as well as the M, N, and P factors. Immunization occurred on account of the so-called "rhesus factor".

Subsequently this work has been substantiated and expanded by other investigators in England and America. It has been shown that the incidence of positive and negative reactions to anti-rhesus serum varied in different races (Table I).

TABLE I.

Race	Percentage of positive reactions
Caucasians	84.5
Negroes	99.9
American Indians	92.9
Chinese	98.5
Japanese	99.0
Filipinos	100.0

Some investigators in genetics suggest that only 85 per cent of the white population is rhesus positive in contrast to all other races, which give a positive reaction in 100 per cent of cases; when rhesus negative individuals have been found amongst these other peoples, the possibility of an admixture of "white" blood has always existed (Potter, 1947).

The clinical importance of this blood factor had been suggested in a previous report by Levine (1939). An interesting case of severe intra-group transfusion reaction occurred shortly after a patient had given birth to an hydropic infant. Cross-matching of her blood serum with many other patients' red-blood cells showed agglutination to occur in the majority of cases. Subsequently the bloods of other patients who had given birth to hydropic infants were tested and similar antibodies to those identified in immunized rabbits

* William Blair Bell Memorial Lecture, delivered to the Royal College of Obstetricians and Gynaecologists, London, on 2nd October, 1948.

were found in many instances. It was suggested that intra-group transfusion reactions could be caused by this rhesus factor antibody. In addition, erythroblastosis foetalis could be explained by the incompatibility between the blood of the intra-uterine foetus and that of its mother. Due to these interesting observations the pathogenesis of two troublesome medical problems was clarified.

My purpose, in this communication, is to discuss the clinical significance of conditions caused by the rhesus factor. Medical journals have been flooded by more than 700 publications during the seven-year period since the rhesus factor was reported as an entity (Potter, 1947). Many of these published observations are inaccurate, while others express unfounded opinions which tend to be misleading. In addition, the early literature on the rhesus factor is confusing because different terminologies are used by the various investigators.

In America the various sub-groups of the rhesus factor have been designated and accepted as Rh_0, Rh′ Rh″ (Wiener, 1943). It should be realized that the rhesus factor is an antigen which can be divided into 3 varieties. Any individual who is rhesus factor positive has blood which possesses some part of the combination; there may be one, two or three varieties present in any rhesus positive person.

Antibodies against this rhesus factor are never a normal constituent of the blood, such as those of the A and B factors. It is only when the rhesus antigen is introduced into the circulation of a rhesus negative individual that antibodies are formed. This is encountered occasionally in clinical medicine with the use of whole-blood transfusions, and in some multiparous pregnancies. Consequently, we know three common anti-rhesus sera, which are designated as anti Rh_0, anti Rh′, and anti Rh″.

Table II shows the various reactions obtained in the Caucasian race using these 3 anti-sera. In addition, it shows the incidence of various rhesus sub-groups as found by these reactions.

TABLE II.

Anti-Rh_0	Anti-Rh′	Anti-Rh″	Rh type (Phenotype)	Percentage incidence
−	−	−	Rh negative	12.3
−	+	−	Rh′	1.1
−	−	+	Rh″	0.9
−	+	+	Rh′ Rh″	0.0
+	−	−	Rh_0	1.1
+	+	−	Rh_1	56.6
+	−	+	Rh_2	16.0
+	+	+	Rh_1 Rh_2	12.0

It was thought originally that the difference between rhesus positive and rhesus negative cells was the presence or absence of rhesus antigens. Subsequent studies have shown that rhesus negative cells do not have a void but possess a weaker antigen, the Hr (Levine, 1945). This was reported by Levine shortly after the 3 anti-rhesus sera were established, at which time he described this anti-Hr serum; Race and Taylor (1943) independently described a similar but more potent serum, which they labelled St.

In an effort to clarify the terminology of the various rhesus factor sub-types, the English group Coombs, Mourant, Race, Fisher, and Cappell (1946) suggested another system of classification. This is known as the Fisher classification and includes the reactions of all these newer blood sera. Table III is a composite of the English and American terminologies. In the earlier investigative stage many of the predicted reactions were purely theoretical. Actually, a large number of these reactions have been proven to exist.

Rh or Hr are inherited by allelic genes. Every individual possesses a pair of genes, one of which is derived from the father, the

TABLE III.

Rhesus Blood Sub-Groups.

	English	American	Rh_1 CDe	Rh_2 cDE	rh cde	Rh_0 cDe	Rh′ Cde	Rh″ cdE	Rh_1Rh_2 CDE	Rh/Rh″ CdE
ANTISERA	Anti-C	Anti-Rh′	+	−	−	−	+	−	+	+
	Anti-D	Anti-Rh_0	+	+	−	+	−	−	+	−
	Anti-E	Anti-Rh″	−	+	−	−	−	+	+	+
	Anti-c	Anti-Hr′	−	+	+	+	−	+	−	−
	Anti-d	Anti-Hr_0	−	−	+	−	+	+	−	+
	Anti-e	Anti-Hr″	+	−	+	+	+	−	−	−

other from the mother. Individuals of pure genotype such as Rh Rh (positive) or rh rh (negative) are homozygous, while those of mixed genotype Rh rh are heterozygous. Because rhesus positivity is considered dominant, all heterozygous individuals are classed as rhesus positive. Consequently, all rhesus negative individuals must be homozygous.

From a practical viewpoint, only those matings where the mother is rhesus negative and the father is rhesus positive should be considered. We are in complete agreement with Levine (1945), in that it is not necessary for the clinician to memorize the various rhesus factor sub-groups and genotypes. In fact, it is in this regard where most medical personnel become confused. Ninety-two per cent of mothers who bear children that have manifestations of haemolytic disease are rhesus negative and the father is rhesus positive. Only the serologist who has specialized training and who has the necessary potent sub-group anti-Rh and -Hr sera is competent to classify the other 8 per cent of cases; these include incompatibilities involving, (1) A and B factors, (2) Hr factor, (3) and the differences between Rh sub-groups.

For these stated reasons the following clinical report chiefly concerns the incompatibility existing between rhesus negative mothers and rhesus positive fathers.

CLINICAL IMPORTANCE.

The majority of medical personnel are familiar with the mechanism of iso-immunization and little should be added in that regard. We know that the rhesus negative woman usually is immunized in two ways, (1) at the time of whole blood transfusion if she receives rhesus positive blood, even though there is ABO group compatibility; (2) the pregnant woman is immunized occasionally by her own foetus when it has inherited the paternal characteristic of being rhesus factor positive. In our opinion this latter type of immunization occurs at the actual time of delivery or when the individual has an abortion.

A general assessment with reference to rhesus factor iso-immunization shows that the incidence is not great. It is obvious that the importance of this condition does not lie in the frequency of its occurrence, but rather in the seriousness of subsequent manifestations when immunization occurs (Philpott, Latour and vanDorsser, 1946). It may prevent the raising of a family of healthy children. There is also a great danger of haemolytic reactions to blood transfusion: however, the risk of creating this latter condition is minimized if the transfusing of rhesus negative individuals is only performed when rhesus negative blood is used. It should be emphasized that one small tranfusion of rhesus positive

TABLE IV.

Foetal Mortality—Royal Victoria Montreal Maternity Hospital, 1941–46.

Foetal mortality 1941–46	Dead born		Died within 24 hours		Died after 24 hours		
Cause	1941–43	1944–46	1941–43	1944–46	1941–43	1944–46	Total
Prematurity { Cause	4	4	11	30	8	8	65
Prematurity { *Associated factor*	(54)	(36)	(16)	(19)	(5)	(11)	(141)
Intrauterine asphyxia	111	103	4	7	2	1	228
Congenital anomalies	46	37	7	5	10	10	115
Intracranial haemorrhage	14	12	17	15	1	7	66
Atelectasis	3	0	18	12	6	7	46
Erythroblastosis	9	8	2	7	3	7	36
Infection	0	0	1	0	0	3	4
Congenital syphilis	2	1	0	0	0	0	3
Cause unknown	3	0	0	5	1	0	9
	192	165	60	81	31	43	572

blood may immunize the rhesus negative woman. As a consequence, this is prone to cause haemolytic reactions with any subsequent transfusion of rhesus positive blood. In addition, it may cause haemolytic disease in her infant even though pregnancy occurs years after the transfusion has been given (Discombe, 1948).

It has been suggested that rhesus negative infants may be immunized at birth by means of the intra-muscular injections of rhesus positive blood. Before the advent of Vitamin K this procedure was common when certain infants were given blood to prevent haemorrhagic diastasis. It is not uncommon for adults to receive injections of whole blood for various complaints. Quite recently we examined the blood of a patient who had received repeated intramuscular injections of whole blood in a futile attempt to cure psoriasis. Her blood showed the presence of blocking and agglutinating antibodies in a dilution of 1:512. This patient happened to have rhesus negative blood. Her husband was the donor and his blood was rhesus factor positive.

Table IV shows all foetal deaths which have occurred in the Royal Victoria Montreal Maternity Hospital during the period from 1941–1946. This includes all babies who died and who were considered to be viable. The cause of death was corroborated by an autopsy examination in 76 per cent of cases. In this six-year period our figures show that haemolytic disease of the newborn is relatively uncommon as a cause of death.

In the two-year period 1946–1947 the laboratory service attached to our hospital completed rhesus factor determinations on the blood of 7,598 pregnant women. Table V gives 1.4 per cent incidence of iso-immunization.

TABLE V.

Antenatal Rh Tests.

Royal Victoria Montreal Maternity Hospital.

1946	4569 cases.	Percentage
	Rh negative	13.2
	Iso-immunized	1.12
1947	3,029 cases	
	Rh negative	14.7
	Iso-immunized	1.7

It is now the rule in our obstetrical clinic that when a patient presents herself for antenatal care, a routine blood examination is completed. This includes red and white blood-cell counts, haemoglobin estimation, serology for the exclusion of

syphilis and the rhesus factor determination.

If the patient's blood proves to be rhesus negative, an attempt is made to test the husband's blood; unless he is proven to be rhesus negative similar to his wife, the patient's blood serum is tested for antibodies of the "agglutinating" (complete) or "blocking" (incomplete) types. These antibody titration tests are repeated with every visit.

During the last 4 years we have completed extensive antibody studies and our results have been published. (Primrose, vanDorsser and Philpott, 1947). The publication includes plotted curves for different grades of iso-immunized individuals.

Grade 1. This shows very slight immunization with low antibody titrations, only becoming evident in the later weeks of pregnancy. The babies are born alive and progress favourably without treatment.

Grade 2. Late appearance of antibodies occurs. There is an elevation of blocking antibodies in the last weeks of pregnancy, but the titration is not above a dilution of 1:8. These babies are born at term showing some clinical signs of erythroblastosis of moderate severity. The blood picture at birth confirms this finding. Infants are usually saved by transfusion and supportive treatment.

Grade 3. During the later weeks of pregnancy there is a sharp rise in blocking antibodies to a dilution of 1:32. There is frequently a sudden drop in the 2 weeks preceding term. The babies are severely damaged but may be salvaged by prompt action immediately after birth.

Grade 4. There is a sharp rise of blocking antibodies in the later months, above a dilution of 1:64, with some agglutinating antibodies, the prognosis for the baby is very poor an account of severe anaemia with oedema. Many of the babies are deadborn if allowed to go to term, death having occurred one or two weeks before delivery.

Grade 5. The appearance of blocking antibodies, sometimes accompanied by agglutinating antibodies, is demonstrated in appreciable concentration of over 1:4 before the 20th week. There is a tendency toward rapid rise in antibody titres. Prognosis is hopeless if the baby is rhesus positive. The result is usually early miscarriage. In the case of a homozygous rhesus positive husband, the prognosis for this family is likely to be uniformly disappointing.

These results suggest the later in pregnancy that antibodies are demonstrated, especially if shown by a low titre, the better is the prognosis. Some curves have been elevated and then have tended to drop in the later weeks. It has been postulated that this drop is caused by increased foetal absorption of antibodies; this is accompanied by a poor prognosis.

It is not the usual occurrence for antibodies to become evident before the last trimester of pregnancy. As an average they appear at about the 30th to the 32nd week. Great care should be taken to keep a close check on titration levels the nearer a patient approaches term. We regard the appearance of the super-added agglutinating antibodies in rising titres as shadowing the prognosis. It is also our opinion that the prognosis is poor in cases where there is a history of previous catastrophes, if there are antibodies demonstrable in early pregnancy.

Treatment.

During the last trimester, if antibody studies show a tendency to become persistently higher or if they suddenly take an appreciable drop, delivery before term should be considered. We prefer to deliver the woman of a premature baby which is definitely viable than to wait and permit

these increasing antibodies to cause widespread destruction of vital tissues in the foetus. It is recognized that premature delivery has its disadvantages, in that the babies born are immature, and that they also show manifestations of the haemolytic disease. However, our personal experience satisfies us that the premature delivery frequently is a life-saving procedure, providing that modern facilities are available for handling premature infants.

The method for delivery should be chosen to suit the individual case. Many of these women are multiparous when the cervix is soft and effaced. In these cases, delivery per vaginam may be the wiser approach. But a hard labour with a difficult delivery is not the best treatment for an ailing baby that is premature, and who has a predisposition to all forms of haemorrhage. If the cervix is firm we think a Caesarean section should be considered.

Where antibodies are demonstrated in any appreciable dilution, certain preparations are made as soon as the patient is admitted to hospital for delivery. These preparations are arranged by a team consisting of a transfusion officer, serologist and pediatrician, who also take charge of the baby immediately after birth. They have at their disposal rhesus negative blood which has been cross-matched against the mother's blood. In addition, there are facilities available to determine certain essentials without delay. These include the haemoglobin estimation, packed cell volume, icteric index, rhesus factor determination, together with any evidence of sensitivity present in the infant's red blood cells. Heparinized cord blood is used. The indicated treatment is carried out according to the results of these tests.

When doing haemoglobin estimations, it is well to remember that cord blood taken at the same time as that from the heel varies on an average of 20 per cent (Philpott, Latour, and vanDorsser, 1946). The cord blood gives the lower reading. In order to avoid erroneous conclusions by comparing cord blood levels at birth with heel punctures at later intervals, it is a wise procedure to make an initial haemoglobin determination with blood taken from the heel.

Many cases of haemolytic disease of the newborn are recognized immediately at birth. These include types such as dead-born macerated infants, the hydropic babies, those with large liver and spleen, and those with marked jaundice. But there are others who do not have such pronounced evidence of the disease and may be classed as the sub-clinical types. These are diagnosed with difficulty or may be recognized only rarely as haemolytic disease of the newborn. Repeated blood studies reveal the definite diagnosis. In addition, one can follow the progress of the disease much better by blood changes than by any other method.

Babies' Blood Changes.

Haematologically, as well as clinically, a number of conditions may simulate haemolytic disease of the newborn (Potter, 1947; Wintrobe, 1947; Blackfan and Diamond, 1944), and successful therapy depends to a large extent upon early diagnosis. This difficulty is increased when haemolytic disease of the newborn is complicated by prematurity. In an intensive study currently in progress at the Royal Victoria Montreal Maternity Hospital; anaemia, marked macrocytosis, large numbers of nucleated and other immature red cells, myelocytes and meta-myelocytes, have been fairly common findings in the blood of normal premature newborn infants. Similar findings have been observed by us and others in birth trauma, haemorrhagic disease of the newborn, babies born of diabetic mothers, conditions producing

anoxia in the newborn such as pulmonary atelectasis, infection in the newborn—especially if associated with impaired liver function—haemorrhage in the newborn from any cause, and congenital syphilis.

There is no single haematologic criterion which permits the diagnosis of haemolytic disease of the newborn. Anaemia, which is usually present or develops shortly after birth, is also found in a number of the conditions mentioned above. The same may be said of large numbers of nucleated red cells, reticulocytes, and other immature forms, as well as the presence of a macrocytosis, (Damashek, Greenwalt and Tat, 1943; Reisner, 1943). Nor do the relative amounts of direct or indirect plasma bilirubin permit accurate diagnosis (Vahlquist, 1944–45). Thus it is realized that early and correct diagnosis in many instances is dependent upon careful clinical assessment, serologic studies of the expectant mother and the newborn baby, thorough haematologic study of the blood of the newborn infant, and at times serial repetition of these studies.

Prognostically, death or survival is not necessarily indicated by the severity and rapidity of development of anaemia and the intensity of the erythropoietic reaction, as reflected by the numbers of nucleated red cells and other young forms present. For instance, one infant made a complete recovery whose blood at birth contained 191,200 nucleated red cells per cubic millimetre; 35 per cent reticulocytes and 60 per cent haemoglobin. Other infants have died with mild anaemia, and with no more nucleated red cells and reticulocytes in their blood at birth than may be found in normal premature newborn infants. There seems to be some correlation between the degree of macrocytosis and survival of the baby. In an established case of haemolytic disease of the newborn, in whom prematurity has been considered, the degree of macrocytosis is probably related to the amount of liver damage.

Severe haemolytic disease can destroy practically all the baby's rhesus-positive cells within the first 24 hours postpartum. The extra-medullary haemopoetic system appears to be inactive for a period after birth; this occurs even when babies are allowed to become anaemic. It is our policy to purposely encourage this inactivity in rhesus positive blood formation by giving repeated large transfusions of rhesus negative blood. The rationale of this procedure is to prevent large amounts of new breakdown products from circulating through the liver. This is inevitable as long as antibodies present in the foetal circulation come in contact with rhesus positive red-blood cells. Breakdown products probably play the role of causative factor of liver damage in this disease.

The acute haemolytic process tapers off in 3 to 5 days. However, the chronic haemolytic stage may be detected for a period of 6 weeks. After that time the condition gradually becomes less marked. We have noted a sudden unexplained drop in the haemoglobin during the second week of life; this occurs even though the antibodies in the baby's blood scarcely can be detected.

Our routine treatment starts as soon as the baby is born and it includes:

1. General supportive measures, such as clearing the air passages, maintaining body temperature by means of suitable incubation, and the continuous administration of oxygen, if indicated.

2. When the baby's blood shows the haemoglobin estimation below 100 per cent, transfusion of whole blood is given within a few minutes of birth. The slow drip method is used most frequently and the blood is given into the temporal vein. There is no syringe pumping.

The usual amount of blood given is 10 ml.

per pound of baby's body weight, but if the blood picture shows a marked anaemia, as much as 25 ml. per pound may be given. One baby weighing 8 pounds, whose haemoglobin was 18 per cent at birth, received 225 ml. of whole blood during the first 4 hours of life. Transfusions are repeated as often as indicated, to maintain the haemoglobin over 100 per cent for the first few days of life.

Anoxia and the usual sequelae such as central nervous system damage and atelectasis are prone to be associated with this severe anaemia. After the fourth day of life one may allow the blood to reach a lower level without too much risk. Many clinicians have thought that if the baby's clinical condition at birth appears good, active therapy is not indicated. Sometimes these babies develop grave symptoms very quickly and therapy is instigated too late.

We have performed several replacement types of transfusion. Five of these exsanguination transfusions were carried out using the original Diamond technique, shortly after birth a long nylon catheter is inserted into the umbilical vein and this extends upward to the vicinity of the right auricle. While using this method our results were poor. We had only one survival and 4 deaths which occurred during the transfusion or within a few minutes of its completion. It should be stated that all 5 cases chosen for this procedure showed marked manifestations of the disease. The usual method of repeated small transfusion has yielded better results. Our recent foetal mortality with this technique is approximately 15 per cent.

A newer method of replacement transfusion has been used to advantage by Diamond and it has also yielded good results in 7 of our cases. Whole blood is administered into the ankle vein, using the cut-down technique. The blood is withdrawn from the umbilical vein by means of a special DuPont Vinylite tip, which is inserted for a distance of 2 inches. This can be performed any time within the first 24 hours of life. In fact, some delay after birth is advantageous. It permits the baby's temperature to reach a normal level and this delay also aids the infant in becoming adjusted to its new environment. Proper balance of blood intake and withdrawal is easily maintained; the average total intake should be approximately 300 ml. against 225 ml. withdrawal. The procedure should not be hurried, and a period of not less than 2 hours is recommended.

Most clinicians interdict nursing of these babies on the surmise that the mother's milk contains antibodies which will cause further blood destruction in the baby. We know that breast milk taken from mothers of the babies with haemolytic disease contains antibodies in high titres. But our experience has shown that milk containing high titrations of antibodies will not cause breakdown of red-blood cells in the nursing baby, absorption of antibodies does not occur. This observation has been corroborated in a recent publication by Cathie (1947).

The "follow-up" of cases born since 1943 has been interesting. This has been divided into 2 periods, the first, 1943–45, and the second, 1946–47. In the first group there were 30 cases which were diagnosed as haemolytic disease (Table VI).

Livebirths include 4 who died within the first week of life and 2 who died from pneumonia at later dates. Included in the 13 cases which are alive, there are 3 who have marked mental retardation and they also have residual spasticity. The 10 normal cases have had no greater incidence of morbidity than other infants of the same age period.

Our second group, Table VII, includes those babies born in 1946–47. There were

TABLES VI AND VII.

Royal Victoria Montreal Maternity Hospital.

Follow-up of Cases, 1943–45.		
Total cases		30
Livebirths	19	
Deadbirths	11	
Neonatal deaths	4	
Later deaths	2	
Alive to-day	13	
Mental and physical retardation ...	3	
Normal		10
Follow up, 1946–47.		
Babies H.D.N. (6–18 mos.)	35	
No trace	1	
Parents' reports only	4	
Full reports	30	
Follow-up, 30 *cases.*		
Mild manifestations at birth	5	
Moderately severe	12	
Severe	13	
Death (congenital heart)	1	
Tardy in walking	1	
Mentally deficient	0	

49 cases of which 8 were deadborn. Thirty-five infants survived and were discharged from hospital. One case could not be traced and there were 4 instances where we have only written reports from the parents stating that these children were normal.

Reports of the remaining 30 cases are satisfactory for accuracy and detail, all being received from pediatricians or from organized baby clinics. These babies range from 6 to 18 months. Five cases were of the mild type and they did not require blood transfusion while in hospital. Progress was normal and they are well at the present time. Twelve babies showed moderately severe manifestations of the disease and they all required one or more blood transfusions during the first three weeks of life. The remaining 13 cases were of the severe types but they were successfully revived by the generous use of rhesus negative blood; three transfusions were of the replacement type.

In general, none of the babies of this second group have been a disappointment to their parents, either in the matter of health or from the standpoint of mental development. Four have recovered from measles or whooping cough. Where routine blood checks were done there was a varying degree of anaemia, this persisted for many months after discharge from hospital despite the good general condition in these babies. In each case the anaemia gradually disappeared under conservative treatment. One baby died at 5 months, death being caused by congenital heart disease and not influenced by the effects of haemolytic disease. Another child is 14 months old and weighs 25 pounds, it has not attempted to walk although it began to sit up at the usual age. The pediatrician who attends this case assures us that its mental and physical development is normal.

Study of both groups impresses one by the high incidence of deadbirths and deaths in the neonatal period. Where the babies survived and were discharged from hospital our results have improved with each succeeding year. Due to these observations we have concentrated on treatment which should tend to improve the condition of the babies at birth. Improved results show that premature delivery has aided considerably when indicated by variations in the antibody titres. In addition, we are investigating another feature of the disease which causes frequent complications and many deaths. Although this work is still in the experimental stage it is worth mentioning.

DAMAGE TO THE LIVER AND THE USE OF METHIONINE.

When the pathological processes involved in haemolytic disease of the newborn were studied from the clinical and post-mortem material, it was obvious that foetal damage to the liver was present in every case. This damage was thought to be long-

lasting, as shown by the follow-up on our cases and by the work of R. J. Drummond and A. C. Watkins in England. They showed that the liver damage in young persons who were thought to be suffering from idiopathic congenital cirrhosis of the liver were really suffering from the late effects of haemolytic disease of the newborn. Taking these facts into consideration it seemed reasonable to attempt the protection of such foetal livers by the use of methionine, whose action as a liver protector had been the subject of so much recent investigational work. Gyorgy's work in animal experimentation showed beneficial results from the use of methionine in conditions which caused widespread liver damage (Gyorgy, 1944). Various reports have shown that there is a possible clinical value in cirrhotic forms of liver impairment (Beams, 1947; Miller, 1947).

Judging from available data on requirements, an arbitrary dosage of 5 g. daily of the crystalline methionine was given to each mother as soon as the first signs of immunization were detected during the pregnancy. This was considered to be greater than the normal maximum daily requirement for a pregnant woman. Such a dose would provide a therapeutic systemic concentration sufficient to deal with moderate liver damage. No attempt was made to assess the woman's daily consumption of methionine in her foodstuffs, and any so obtained was regarded as a supplement.

During the course of foetal development, as the need for methionine was manifested, the positive balance available in the maternal organism would be drawn across the placenta by the foetus. This is in accord with the generally accepted theory of foetal demand and maternal supply. Since methionine is an essential amino-acid its passage across the placenta would be uninhibited.

When receiving methionine the mothers were seen every 2 weeks before the birth of their babies. A constant check was made on their consumption of the drug and on the antibody blood levels. No case of idiosyncrasy or untoward reaction to the drug was noticed and no patient had to discontinue taking the drug because of nausea. Some complained in having to take 10 fairly large tablets day after day. In some cases treatment was carried over a period of more than 150 days, a total of approximately 1,000 g. (Philpott and Primrose, 1948, to be published).

In milder stages, grades 1 and 2, where antibody levels in the blood were low the use of methionine was not advised, as we were confident that the babies would do well without treatment. However, quite arbitarily, a single case was selected in Grade 1, and three in Grade 2, and the others were used as controls. When it was obvious that any case was going to fall into the more serious Grades, 3, 4, or 5, a most intensive effort was made to talk the mothers into taking methionine with the assurance that we hoped by this means to obtain a live baby. All clinic cases were offered the chance but in each group a certain proportion could not be so persuaded. These cases, together with a few private patients whose doctors chose to carry on with observation of the titrations but without methionine, formed a convenient source of controls. The only other medication given these patients was a ferrous sulphate preparation of iron and a multiple vitamine capsule, both in routine use in our clinic.

Every case of haemolytic disease during the year 1947 and up to 1st May, 1948, is included in this report.

The deadborn group were subjected to careful pathological examination and the nature of their disease was studied. Samples of cord blood from the liveborn group were examined and the presence of

haemolytic disease of the newborn was confirmed. This cord blood was examined in every case by a battery of liver function tests. Each baby was examined by at least 2 paediatricians and at no time before examination did they know whether a baby was receiving methionine or was a control case. Of the liver studies available only the cephalin-cholesterol flocculation was consistently affected in the severe cases.

Within the limits of the quantity of material available, 50 cases, the original premise is considered vindicated as shown in Table VIII.

chemical studies show a noteworthy difference between the two grades. The difference is most marked in the severe Grades 3, 4, and 5. In these 3 groups 19 control cases had one survivor or 5 per cent survival rate. Of the 12 cases receiving methionine, 10 babies were born alive, and 8 survived, giving a gross survival rate of 66 per cent.

It should be emphasized that in this disease we are using methionine purely as a liver protective. We know that antibody development occurs as usual in the mother and haemolysis of the red-blood cells occurs

TABLE VIII.

Results with Methionine in the Royal Victoria Montreal Maternity Hospital.

Grade		Cases	Dead born	Alive born	Survived	State of liver	Cephalin-cholesterol
I.	Control	10	nil	10	10	Slight to moderate liver enlargement	+++
	Methionine	1	nil	1	1	No liver enlargement	neg.
II.	Control	3	nil	3	3	Palpable liver and spleen	+++
	Methionine	3	nil	3	3	No liver or spleen palpable	+
III.	Control	3	2	1	1	Liver and spleen enlarged +++	+++
	Methionine	4	nil	4	4	Liver and spleen just palpable	+ to ++
IV.	Control	4	4	nil	nil	Advanced erythroblastosis	?
	Methionine	3	1	2	nil	Slight liver and spleen enlargement	++
V.	Control	9	8	1	nil	Hydrops, etc., aborted	?
	Methionine	5	1	4	4	Liver and spleen just palpable	++

Control—Control cases.
Methionine—Methionine cases.

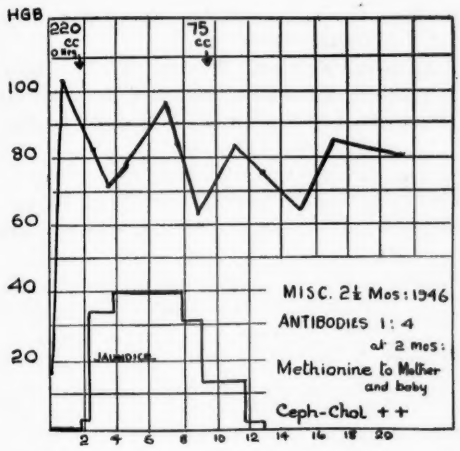
The cases have been divided into grades, and the methionine group has been compared with the control group. The results reveal a striking difference between the control group and those receiving methionine. No claim is made for any significant difference in the survival-rate of Grades 1 and 2; although both the clinical and bio-

in the foetus. Our point is that we can treat severe anaemia in the newborn but we cannot adequately treat a severely damaged liver.

One baby in this series had a haemoglobin of 18 per cent and a corresponding low red-cell count, but it responded well to transfusion treatment because the liver was

not severely damaged. The cephalin-cholesterol test showed only minor impairment (Table IX).

TABLE IX.



All babies who are diagnosed as haemolytic disease receive ½ g. of methionine daily for at least the first 12 days of life. This is given .125 g. in 5 per cent glucose saline or in the milk. Practically all the babies have taken this mixture with avidity, almost denoting that they required it in their systems.

Prevention is the best treatment whenever it is possible. Relative to rhesus iso-immunization this could be accomplished on our present knowledge only by premarital typing of partners and advice against marriage of the woman who has rhesus negative blood with the man who possesses rhesus positive blood. For obvious reasons this would not be feasible: realizing that first babies are rarely affected by this disease, one could consider advising incompatible couples to limit the family to one offspring, but this suggestion is also impractical.

Experimental treatment of a prophylactic nature includes an attempt to suppress formation of the rhesus antibody by injecting a stronger antigen such as typhoid or pertussis vaccine. Reactions to this therapy are troublesome, especially in the pregnant patient, and there are no apparent beneficial results. Drugs which are related to the anti-histamine groups (ethylene disulphonate) have been used, but further study is necessary to prove any benefit from their use (Kariher and Miller, 1947).

Specific action should be obtained when certain substances such as "haptens" are extracted (Levine, 1946). These have the power to neutralize antibodies without being antigenic themselves. In this manner a woman who has quantities of circulating antibodies could be freed of the danger of harming her own child (Carter, 1948). Dr. Carter presented an interesting paper in August 1948 at the meeting of the American Association of Blood Banks, this was referable to the extracting of "haptens" by a simple precipitation method. It is claimed that these haptens have the property of neutralizing the rhesus antibodies.

When there is a history of repeated tragedies and the wife is rhesus factor negative with the husband rhesus factor homozygous positive, means should be afforded to prevent subsequent pregnancies. In addition, the general assessment of this problem makes one pause to consider the advisability of trying to save the pronounced case of haemolytic disease in the newborn. Under proper supervision mild cases progress favourably, but in those cases who have severe manifestations and who survive there is a moderately high incidence of physical and mental defects. When such cases occur it is most disturbing. However, our "follow-up" of cases shows that these can be prevented by prompt and adequate treatment. A recent brilliant article by Cappell (1948) also emphasizes this point.

Conclusions.

1. Importance of iso-immunization does not lie in its frequency but rather in the seriousness of subsequent manifestations.

2. Antenatal antibody studies aid in making a prognosis. Premature delivery may be indicated by variations in titration levels.

3. The liberal use of rhesus negative blood, if indicated, frequently prevents immediate or remote complications in the infant.

4. Foetal liver damage plays an important role in the progress of the disease. The use of methionine has been used as a liver protective with apparent good results.

I wish to express my sincere thanks to the Department of Pediatrics, Dr. Louis Lowenstein, our haematologist, Doctors J. P. A. Latour and Thomas Primrose for their co-operation and assistance in preparing this paper.

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MASSIVE LYMPHANGIOMA OF THE FOETAL TRUNK AND SHOULDERS CAUSING DYSTOCIA

Report of a Case

BY

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IMPACTION of the shoulder girdle in head presentations is a rather uncommon complication of labour, although not so rare as one might assume from the scanty attention given it in many of the text-books of obstetrics. It is most likely to occur when the foetus is unduly large, because the circumference of the shoulder-girdle of the oversized infant is proportionally greater in relation to the circumference of the head than is that of the normal or small one. Dystocia due to abnormal local enlargement of the shoulders occurs rarely, so the following case may be of some interest

A woman aged 32 years, 2-para, 3-gravida, was seen at the antenatal clinic of the Winnipeg General Hospital on 16th August, 1940. Her past medical history was not remarkable. The 2 previous deliveries, in 1934 and 1936, were said to have been normal. The present pregnancy had apparently been uneventful save for slight oedema of the ankles during the last month. Her blood-pressure was 124/84. She refused further physical examination.

The membranes ruptured spontaneously on 24th August, at term. The patient thought the amount of liquor amnii was excessive. Labour began 7 hours later. At the first examination after admission to hospital the presentation was found to be vertex, the position right occipito-anterior, and rectal examination confirmed that the head was engaged in the pelvis and the cervix dilating. Progress was rapid and she was taken to the delivery room, with the caput showing, less than 2 hours after the onset of labour. The occiput had rotated forward. Light chloroform-ether analgesia was given with the pains, and the head descended normally until its greatest diameter was just past the vulva. At this point descent ceased, and it was necessary to push the perineum up past the face in order to clear the baby's mouth. The uterine contractions continued strong and frequent but the head came no further down. The foetal heart-sounds became slow and irregular and the head deeply cyanosed. The patient was fully anaesthetized, a wide left mediolateral episiotomy was done, and the cause of the obstruction was sought. The anterior (left) shoulder could be felt overriding the symphysis pubis. Attempts were made to push it behind the symphysis by supra-pubic pressure but it would neither descend nor rotate laterally into the oblique diameter of the pelvis. The anterior axilla was sought in the hope of using it for traction, but it could not be identified as the bony landmarks were obscured by loose flabby tissue. In the meantime the foetal heart had stopped.

Upon the arrival of the senior author the patient was placed in the left lateral (Sims's) position, the genitalia cleansed and re-draped, and the patient again deeply anaesthetized. With the left hand inserted high in the vagina behind the head it was possible to identify the posterior (right) arm, and, after disimpacting the shoulders somewhat by upward pressure, to bring it down in front of the

child's chest and past the head. A strong pull on the arm brought the posterior shoulder almost to the outlet; then traction on the head and arm, directed well posteriorly, brought the anterior shoulder under the symphysis and delivery was easily completed. The third stage of labour was uneventful. The episiotomy had fortunately not extended unduly and was repaired.

Convalescence was quite uneventful save for urinary retention which made catheterization necessary until the fifth postpartum day. As she had in the antenatal clinic, the patient modestly but firmly refused physical examination at the time of her discharge from the ward.

The child, a male weighing 9 pounds 4 ounces (4195 g.), showed a marked deformity of the upper part of the body, which was largely covered by multiple, loose, partially pedunculated tumours as shown in the photograph (Fig. 1). On the left the tumours involved the anterior aspect of the upper arm, the axilla, and the upper part of the chest wall: on the right they covered the entire upper arm and axilla and the side of the thorax down to the crest of the ilium. The margins of the masses were poorly defined. The growths at first glance suggested lipomata, but on closer examination were found to be cystic, the overlying skin being so thin in some places that the cysts could be seen shining through. On dissection multiple smooth-walled spaces were found, varying in size from pin-point to 3 cm. in diameter. In some the fluid was yellow and coagulated, in others thin and watery, and in some blood-stained. On microscopic section the tumour was found to be a typical lymphangioma. All other organs were grossly normal, save for the lungs which were completely atalectatic and showed many petechial haemorrhages.

The great increase in bulk of the shoulder girdle is well shown in the photograph. The true bisacromial diameter was 13 cm., not abnormally large for the size of the child, but when the tumour was included the diameter across the upper arms was 18 cm. An onlooker remarked that the child looked like an American football player wearing pads!

Literature.

Congenital lymphangiomata are not excessively rare, and may be present at birth or appear later. In a series of 28 cases presented by Singleton (1937), 16 were present at birth. The origin of these tumours is a matter of speculation. Early human embryos show 6 lymph sacs, 2 in the posterior abdominal wall, the other 4 at the roots of the 4 limbs. Those at the roots of the arms are called the jugular lymph sacs (Brash, 1943). Subsequently these sacs become converted into plexuses of lymphatics and into the vascular lymph-nodes. There are two views concerning the development of the more peripheral lymph-vessels: according to one view they arise by direct centrifugal extension from the endothelium of the lymph-sacs: according to the other view they arise *in situ* by transformation of mesenchymal lymphangioblasts into lymphatic endothelium, and develop secondary central connections with the direct derivatives of the sacs. The latter view seems the more helpful in the attempt to understand congenital lymphangiomata.

Singleton (1937), in an excellent discussion of lymphangiomata, divides them into 3 types: (*a*) simple or capillary, (*b*) cavernous, and (*c*) cystic. The distinction between the latter 2 groups appears to be mainly in the size of the cyst spaces. They can arise wherever a lymph-sac has existed. He considers them to be true blastomata, arising from undifferentiated mesenchyme capable of producing lymphatic vessels by activity and growth of lymphangioblasts. These vessels may be blocked later or be congenitally blind. It is very probable that normal-functioning lymphatics do not change to become involved in tumour development. The distribution of the tumours in the present case is consistent with development from the areas of distribution of the 2 jugular sacs.

From the obstetrical viewpoint, congenital lymphangiomata seldom cause serious delay in labour. Berkeley, Bonney and MacLeod (1938) state that most infants

with lymphangioma or cystic hygroma are females and are usually born prematurely. Sheares (1941), in a comprehensive review of foetal abnormalities causing difficult labour, says that "congenital tumours of the shoulders are mentioned in the literature, but no case causing dystocia has been described." Singleton (1937), however, discusses the case of a child having a large cavernous lymphangioma the size of a foetal head in the left axilla, which was so large that decapitation and puncture of the tumour were necessary before delivery could be completed. McPherson (1917) reported the delivery of a child with a multilocular cystic tumour involving the entire left side of the thorax and the greater part of the arm. It had not caused any difficulty in the delivery. Ealing (1943) recorded the case of a child with a large congenital haemangioma, 9 inches in circumference, extending above and below one elbow, which caused delay in delivery until the arm had been freed. The child died after 3 days and was found to have a much dilated heart, which one assumes to have been the result of an arteriovenous shunt through the highly vascular tumour. Dystocia is more often caused by angiomata of the neck (cystic hygromata), which may interfere with normal flexion of the head, as in Johnstone's (1932–33) case. This was, incidentally, the only tumour of the neck large enough to cause dystocia encountered in over 50,000 deliveries at the Royal Maternity Hospital, Edinburgh. Szerb (1936) described a case in which a cystic lymphangioma the size of a foetal head, situated between the right ear and shoulder, was successfully removed 31 hours after birth. The growth had caused considerable difficulty in a breech delivery.

Discussion.

Dystocia due to impacted shoulders deserves more attention than many obstetric texts give it. It can be a real emergency and one which must be dealt with in the vitally important few minutes before the child dies of asphyxia. The multiplicity of manoeuvres advocated reveals the unfortunate fact that the mechanism of descent and rotation of the shoulder girdle is poorly understood and indeed does not seem to have been adequately investigated. Without a knowledge of the normal mechanisms and their possible variations assistance must be empirical. Too often the convenience of the delivered head as a "handle" leads to the use of undue force, causing permanent damage to the brachial plexus or injury of the cervical vertebrae and their ligaments. Often merely rotating the shoulder girdle into the transverse or an oblique diameter of the pelvic brim will suffice, and pressure on the anterior shoulder may accomplish this. Bringing down an arm, usually the posterior one, substitutes for the bisacromial diameter the axillo-acromial, said by Audebert (1934) to be 2 to 3 cm. less. The case here described shows the success of this manoeuvre, but it is not easy to do, especially when the posterior portion of the pelvic cavity is small and the hand cannot be introduced easily. Munro Kerr (1937) stresses the advantage of the Sims's position when manual correction of faulty position is attempted. Manly (1929), Brown (1933), Woods (1934), Barnum (1945) and McCormick (1947) have described methods of releasing impacted shoulders by rotation of the body of the foetus through a half-circle, with or without bringing down an arm first. It seems very logical if one visualizes the shoulder girdle threading its way through the pelvis with a screw-like motion. As a final resort, usually after the death of the foetus, one may resort to cleidotomy to diminish the breadth of the shoulder girdle, though sometimes even this is not enough to release the obstruction.

In the present case, after early rupture of the membranes, the lower uterine segment was so closely wrapped around the fleshy foetal shoulders as to prevent their rotation. It may be argued that, as the child was dead, bilateral cleidotomy would have made delivery possible without the need for bringing down an arm, a difficult feat and not without risk even when carefully done. But identification of the clavicles is not easy, and was made more difficult here as they were obscured by the overlying tumours. Blind seeking with the scissors would have involved greater risk of damage to the maternal tissues.

Summary.

A case of impaction of the shoulders due to a congenital cystic lymphangioma is described. The recent literature on congenital lymphangiomata and their effect on labour is touched upon. Methods of dealing with impacted shoulders are briefly considered, especially as they apply to the management of the case described.

The description of the tumour is adapted from a report by the late Dr. Sara Meltzer, Assistant Pathologist, Winnipeg General Hospital. We are indebted to Professor I. M. Thompson, Department of Anatomy, University of Manitoba, for assistance in the discussion of the embryology of the lymphatics.

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FIG. 1

Photograph of foetus showing the distribution of the multiple lymphangiomata

R.B.M. & D.B.S.

CALCIUM AND PHOSPHORUS METABOLISM IN PREGNANCY

(A Survey under War and Post-War Conditions)

VI. Postnatal Findings

BY

E. Obermer, M.D., M.R.C.S.

Fifty-three healthy pregnant women were originally selected for this survey. Their calcium intake, output and balance figures, together with tables and a discussion of both calcium and phosphorus balances throughout pregnancy, have been given in the first three papers of this series (Obermer, 1946a, 1946b, 1947a).

In 5 cases the experiment had to be discontinued in the early stages of pregnancy. The antenatal and labour findings of the remaining 48 cases were discussed in relation to the calcium and phosphorus balances, in papers IV and V of this series (Obermer 1947b, 1948). The reader is referred to these two papers for (*a*) a discussion of the reasons for the division of the cases into 7 groups and (*b*) details of the exact dosage of the supplements. The same plan is adhered to in the present paper.

The postnatal findings are divided into the same 7 groups:

Group A. Controls.
,, B. Supplement of "colloidal" calcium phosphate.
,, C. As B, together with large doses of Calciferol.
,, D. Supplement of calcium phosphate B.P.
,, E. As D, together with the same large doses of Calciferol as C.
,, F. Supplement of Calciferol only—in varying doses, all relatively small.
,, G. Supplement of Calciferol only—in varying larger doses.

The group findings can be compared with the calcium and phosphorus balances during pregnancy by referring to Table I, reproduced from Paper V.

Table I.
Total Maternal Loss or Gain of Calcium and Phosphorus throughout Pregnancy. Mean for each Group (Expressed in g.)

Group	Number of cases	Calcium			Phosphorus		
		Balance throughout pregnancy	Content of foetus	Total maternal loss or gain	Balance throughout pregnancy	Content of foetus	Total maternal loss or gain
A	6	−135	25	−160	+28	14	+14
B	6	− 20	25	− 45	+42	14	+28
C	7	+ 17	25	− 8	+90	14	+76
D	6	+ 1	25	− 24	−11	14	−25
E	6	− 1	25	− 26	+36	14	+22
F	10	− 90	25	−115	− 0.5	14	−14.5
G	7	− 45	25	− 70	+17	14	+ 3

TABLE II.

Group	Case No.	Duration of lactation	Mother's health during first year	Baby's health during first year
A	1	2 months	Good	Bronchitis 4 months
	2	7 ,,	Good	Good
	4	3 ,,	Breast abscess 1 month, otherwise good	Good
	5	9 ,,	Very good	Good
	6	6 ,,	Very good	Very good
B	13	5 ,,	Fair—tired	Good
	14	4 ,,	Good	Very good
	16	7 ,,	Fair—tired	Very good
	17	3 weeks	Good	Good—chilblains at 6 months
	18	5 months	Fair—tired	Good
C	25	9 ,,	Very fair—slightly tired	Very good
	26	5 ,,	Good	Very good
	27	1 ,,	Good	Good
	28	5½ ,,	Fair—bad sleep owing to bombing	Fair—poor sleep
	29	5½ ,,	Fair—tired	Fair—poor sleep, bronchitis 6 months
	30	5 ,,	Good	Fair—poor sleep
D	19	7 ,,	Fair	Good to 7 months, then flabby and catarrhal
	20	6 weeks	Good	Good
	21	9 months	Good	Good
	22	6½ ,,	Good	Good
	54	4½ ,,	Good except for headaches	Very fair—irritable at night
	23	5 ,,	Very fair—slightly tired	Very good
E	33	6 ,,	Very fair—slightly tired	Very good
	34	Nil	Fair—tired	Good
	36	6 months	Fair—tired	Fair—bronchitis 7 months
F	39	3 ,,	Very fair—tired	Good until 8 months—croup
	40	4½ ,,	Good	Very good
	41	4 ,,	Good	Very good
	43	7½ ,,	Fair—tired	Good
	44	9 ,,	Good	Very good
	45	2 ,,	Poor—very tired	Very good
	46	6 ,,	Very fair—slightly tired	Very good
G	47	5½ ,,	Good	Good
	48	4 weeks	Poor—very tired	Good
	49	8 months	Good	Very good
	50	1 week	Very good	Very good
	51	6 months	Very good	Very good
	52	3 ,,	Fair—pyelitis—slightly tired	Very good
	53	Nil	Very good	Very good

Postnatal Findings.

Of the 48 cases observed throughout pregnancy one case (case 3, Group A) had a stillborn baby and 2 (cases 38 and 41, Group F) had twins—a total of 49 babies. This figure was reduced to 48 by a neonatal death (from pneumonia) in case 35, Group E.

Details as to infant feeding and as to the progress of mother and baby were collected on a postnatal form sent to each mother. This form was, of course, not filled out by cases 3 and 35. Two cases refused to fill out the form and 5 others were lost sight of, as they had moved away from London during the post-war period. Rough postnatal notes on the remaining 39 women are given in Table II.

Infant Weight Chart.

Of the 39 cases covered by Table II one only (case 41, Group F) had twins—a total of 40 infants. Weight charts were graphed out for 38 of these 40 infants. In a few instances the figures on the postnatal forms were given by the mothers themselves. The majority were supplied by infant welfare centres. In 2 cases the figures were mislaid.

The birth-weights have already been discussed (Obermer 1948, p. 144). The weights at 6 months and 1 year respectively are given in Tables III and IV.

Table III.

Group	No. of cases	Weight at 6 months: Mean lb.	oz.	g.	Minimum lb.	oz.	g.	Maximum lb.	oz.	g.
A	5	17	6 4/5	7900	14	0	6350	22	1	10000
B	5	17	5 1/5	7855	14	6	6520	20	0	9100
C	5	16	10 2/5	7600	13	3	5980	17	13	8070
D	6	17	5 2/3	7870	14	8	6580	19	0	8665
E	3	16	8	7530	14	12	6465	17	12	8040
F	7	16	2 3/7	7375	14	2	6180	19	8	8880
G	7	17	1 1/7	7785	15	0	6810	18	7	8410

Table IV.

Group	No. of cases	Weight at 1 year: Mean lb.	oz.	g.	Minimum lb.	oz.	g.	Maximum lb.	oz.	g.
A	5	22	5 3/10	10,115	17	0 1/2	7,700	28	0	12,600
B	5	23	6 2/5	10,600	20	12	9,440	29	0	13,055
C	3	23	12 2/3	10,770	21	8	9,780	27	6	12,315
D	4	22	10 1/2	10,260	21	12	9,895	23	12	10,750
E	2*	22	0	9,970	22	0	9,970	22	0	9,970
F	6	19	12 1/3	8,985	17	12	8,025	22	6	10,140
G	6	22	7 1/6	10,170	21	0	9,550	23	8	10,635

In view of the large number of factors involved in growth it is not surprising that there is no significant difference in the mean weights for the different groups.

When the figures for the increase in weight of each individual infant were plotted out against the average 48-hour ± calcium and phosphorus balances of the mother no correlation could be found. This was done for the increase in weight from

birth to the 12th week, 13th to 16th week, 17th to 26th week, 27th to 52nd week.

A comparison of the mean group increases at these different periods of the first year, however, showed definite differences. The numbers are too few to be statistically significant, but they are sufficiently marked to warrant tabulating (Tables V, VI, VII and VIII).

The mean figure for Group A in Table V is misleading. The baby in case 6 actually gained 10 pounds 6 ounces (4,700 g.) from birth to 12 weeks. Case 6 was an exceptionally healthy and vigorous young woman and her husband was a young man in the American Air Force—a splendid physical specimen. If this baby were omitted from the group the mean for Group A would be 5 pounds 4 ounces (2,380 g.). This would make the Group C mean increase greater than all the other groups.

The figures in Table VI show an increase

TABLE V.

		Increase in Weight—Birth to 12th week								
		Mean			Minimum			Maximum		
Group	No. of cases	lb.	oz.	g.	lb.	oz.	g.	lb.	oz.	g.
A	5	6	4	2835	4	6	2000	10	6	4700
B	5	5	6	2440	2	7	1100	6	11	3040
C	6	5	15	2695	3	15	1780	6	12	3065
D	6	5	3	2350	4	0	1805	6	7	2920
E	3	4	11	2120	3	13½	1740	5	10	2555
F	8	4	10	2090	2	10	1190	5	9	2530
G	7	4	11½	2135	1	9½	720	6	6	2890

TABLE VI.

		Increase in weight—13th to 16th week								
		Mean			Minimum			Maximum		
Group	No. of cases	lb.	oz.	g.	lb.	oz.	g.	lb.	oz.	g.
A	5	1	4	570	0	11	310	2	3	990
B	5	1	9	710	0	15	425	2	6	1080
C	6	1	10 1/3	740	0	14	400	2	7	1105
D	6	1	5	595	1	0	455	1	9	710
E	3	1	9	710	1	7	650	1	12	795
F	8	1	9 3/8	720	1	0	455	2	3	990
G	7	1	7 1/7	655	1	0	455	1	15	880

TABLE VII.

		Increase in weight—17th to 26th week.								
		Mean			Minimum			Maximum		
Group	No. of cases	lb.	oz.	g.	lb.	oz.	g.	lb.	oz.	g.
A	5	2	10 4/5	1210	2	4	1020	2	13	1275
B	5	3	0 3/5	1375	2	3	990	4	10	2100
C	5	2	13 1/5	1280	1	4	565	4	7	2015
D	6	3	3 1/2	1460	1	11	765	4	15	2245
E	3	3	5 1/3	1520	3	0	1360	3	8	1590
F	7	3	9 2/7	1620	1	11	765	5	12	2600
G	7	3	8 4/7	1605	2	8	1130	4	6	1990

TABLE VIII.

Group	No. of cases	Increase in weight—27th to 52nd week. Mean lb.	oz.	g.	Minimum lb.	oz.	g.	Maximum lb.	oz.	g.
A	5	4	14 1/2	2230	3	0 1/2	1370	5	15	2680
B	5	6	1 1/5	2750	3	4	1470	9	0	4100
C	3	6	4 1/3	2840	4	8	2040	9	9	4355
D	4	5	15	2680	5	1	2300	7	0	3180
E	2	4	11	2125	4	4	1935	5	2	2325
F	6	4	3 1/6	1910	2	12	1250	5	3	2355
G	6	5	2 5/6	2355	4	8	2040	6	0	2720

for Group C which is definitely higher than the others. This implies a correlation between the group means and the mean maternal loss or gain of calcium and phosphorus during pregnancy, as shown in Table I.

Table VII also shows the lowest increase of all groups for Group A (control). During this period the majority of mothers were still breast feeding. The largest mean increases were shown by Groups F and G—supplements of Calciferol only during pregnancy.

Table VIII covers a period when most of the infants were on bottle or mixed feeding. Only a few were breast fed during the first part of this period—see Table II. The factors involved are therefore more numerous and complex. Nevertheless, the mean increase for the control Group A is again the lowest, except for Groups E and F. Group E could be legitimately eliminated from this table, as the weights for two infants only were known for this period. The figures for group F are also partially invalidated by the fact that one of the twins (case 41) almost stopped gaining weight after the 7th month.

DISCUSSION.

Far too little is known about the influence of calcium and phosphorus metabolism during pregnancy or lactation and postnatal development. That some influence must be exerted can be deduced from what evidence we possess as to maternal calcium and phosphorus metabolism during lactation. All the findings (Blunt and Cowan, 1930; Hunscher, 1930; Macy *et al.* 1930, 1934; Mendenhall and Drake, 1934) point to a constant calcium depletion of the mother throughout lactation, though phosphorus depletion is less frequent. Shohl (1939) points out that a generous intake of calcium and vitamin D might sufficiently increase the storage during pregnancy so that "lactation would not cause depletion beyond the normal or might maintain the calcium reserves throughout." Much more work has been done on cows and goats. Some of the literature is given by Crichton (1930). Some idea of the scope of American work on this subject can be arrived at by referring to Ellenberger *et al.* (1932), Hart *et al.* (1930) and Meigs *et al.* (1935). The evidence is suggestive, but not as yet conclusive, that large mineral and Calciferol supplements improve both the quantity and the quality of the milk, the maternal resistance to disease, and increase the growth-rate of calves. Even in this field, however, we do not know enough to understand the exact role of the different factors involved.

In the present survey it was not possible to persuade the women to carry out test periods during lactation. This would have involved further weighing and measuring

of food and drink and the sampling of breast milk. The average working-class mother does not take too kindly to experimental work. The women could be persuaded to take a lot of trouble during pregnancy. They had plenty of spare time, and those who were given supplements were convinced that the baby would benefit. During lactation, however, they were kept too busy "looking after baby" to consider further experimental co-operation. It can be assumed, however, that their diets were similar to those consumed during pregnancy, minus the supplements. In all cases, therefore, it is probable that the calcium intake during lactation was suboptimal, if one accepts the figure given by Holmes (1945) of a minimum calcium requirement of 1.58 g. per day for a 59 kg. lactating woman. The same author's phosphorus requirement of 1.36 g. per day was probably met in the majority of these cases.

The mean group weight increase figures given in the tables show differences which are suggestive, in the light of the little that we know and the more that we are entitled to assume. These differences are born out by the weight graphs which will be published later. The general tendency of the weight lines of the infants, whose mothers had received supplements during pregnancy, was towards a more regular "straight line" progression. The mean weight increase of the A or control group was definitely lower for all the periods, except from birth to the 12th week. The possible explanation of this anomaly has been given above. Group C mothers showed the lowest net maternal loss of calcium and the highest gain of phosphorus during pregnancy. Group C infants showed the highest weight increases, both from the 13th to 16th week and from the 27th to 52nd week, and the second highest from birth to the 12th week. It must be emphasized, once more, that the numbers are too few to be of any statistical significance. That there are suggestive differences, however, in the different groups should encourage others to carry out similar experiments, in a more comprehensive manner and on a much larger group of cases. There can be no question about the great importance of calcium and phosphorus metabolism for mother and child, both during pregnancy and lactation. Adequate data to clarify the subject are urgently needed.

Summary.

1. Brief postnatal data are given for 39 out of the 53 women who took part in this survey, divided into 7 groups—1 control and 6 given supplements of calcium and phosphate and/or Calciferol.

2. The weight charts of 38 infants, divided into the same groups, are discussed.

3. No correlation could be found between the average 48-hour loss or gain of calcium and phosphorus of the mother during pregnancy and the increase in weight, as shown on the individual infant's weight chart.

4. No correlation could be found between the maternal findings during pregnancy and the mean group weights of the infants at 6 months and 1 year.

5. The mean group weight increases are given, in tabular form and divided into periods—birth to 12th week, 13th week to 16th week, 17th week to 26th week, 27th week to 52nd week.

6. With a single exception the mean weight increases for the A or control group were lower than for the supplemented groups.

7. The mean weight increases for Group C—the group in which there was the least maternal loss of calcium and the maximum retention of phosphorus during pregnancy—were greater than all other groups from the 13th to 16th week and from the 27th to

52nd week, and the second highest from birth to 12th week.

8. Stress is laid upon the fact that the numbers are too few to be of statistical significance. Nevertheless, our knowledge on this subject is so deficient that a few accurate data are considered worthy of publication. The hope is expressed that these suggestive findings will be confirmed or invalidated by experiments on a larger scale.

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NORMAL PREGNANCY IN A CASE OF THROMBOSIS OF THE INFERIOR VENA CAVA

BY

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RECOGNITION and reporting of cases of thrombosis of the inferior vena cava, which used to be thought a very rare condition, has revealed an incidence higher than commonly estimated. One of the earliest records in the literature of this condition was in 1644, when Schenck described 2 cases which he found at necropsy. Bottini in 1893 appears to be one of the earliest surgeons who successfully ligated the inferior vena cava, the patient making a complete recovery without any complications. Jacob Hall Pleasants (1911) published a report of 18 cases diagnosed from amongst 400,000 patients admitted to the Johns Hopkins Hospital during the previous 20 years. Four of these patients had developed thrombosis of the inferior vena cava following puerperal sepsis (which after neoplasm he cited as the commonest cause) and, after studying in addition 41 similar cases quoted in the literature, Pleasants found that out of this total of 45, only 1 patient survived.

The present case of thrombosis of the inferior vena cava following pelvic cellulitis in a woman in whom conception occurred 10 years later, with subsequent normal delivery of a live child, is therefore of interest.

CASE RECORD.

The patient was aged 39, married, and her occupation was a club reception-clerk. She had previously given birth to 3 babies at term and a 4th prematurely at 7 months' gestation following antepartum haemorrhage in 1931. She was admitted to the surgical department of the Postgraduate Medical School of London in October 1947 complaining of haemorrhoids. A history was given of their developing after the birth of her first baby in 1926. In 1938 a haemorrhoidectomy and also a uterine curettage had been performed in a cottage hospital and, after these operations, she developed pelvic cellulitis, which detained her in hospital for 6 months. She stated that during most of this time the legs were swollen. She appeared to have recovered successfully, but 2 years later varicose ulcers broke out about the ankles. In 1943 she had an abortion at 8 weeks, and in 1946 another abortion, and for treatment of this was admitted to a London hospital where marked superficial varicositis were observed on the abdomen.

Upon general examination by us, in October 1947, large veins were noted coursing over the lower abdomen around to the flank and over the upper abdomen pursuing to the chest, the direction of the flow being headwards. The liver was not enlarged and the spleen was not palpable. Both legs showed moderate-sized varicose veins, and some oedema.

Proctoscopy revealed engorged internal haemorrhoids. The heart was normal in all respects, and the blood-pressure was 130/90. The diagnosis of thrombosis of the inferior vena cava was therefore made. A brownish vaginal discharge, however, attracted attention to the genital organs, where examination revealed the presence of a 5-months gestation and a small fibroid. She discharged herself from hospital at her own risk in December.

Five weeks later (12th January, 1948), she was admitted for observation and assessment of her physical ability to continue the pregnancy. Intravenous pyelography revealed satisfactory excretion in both kidneys; the Van den Bergh direct reaction was negative and the absence of bile in the urine excluded any liver morbidity. A catheter specimen of urine revealed pus cells, and a heavy growth of *Streptococcus faecalis* was cultured. The blood was Rh negative, and the haemoglobin content 64 per cent (Haden): 10 g. per 100 ml. The volume of fluid output relative to fluid intake was within normal limits. The varicosities in the anterior abdominal wall and legs were becoming more marked. It was decided to give the patient complete rest in bed and let the pregnancy continue.

Four weeks later (17th February), a phlebogram was performed by introducing 20 ml. diodone through a ureteric catheter into the right internal saphenous vein, at the saphenous ring (Stowers and Grossman, 1946). It was only found possible to introduce the catheter 4 inches. Unfortunately the skiagram was not satisfactory. At 24 weeks infra-red photographs were taken to show the varicosity of the anterior abdominal wall (Figs. 1 and 2).

The urine was albumin-free throughout her stay in hospital except during mild exacerbations of right-sided pyelitis which caused the patient some distress from time to time, and she also suffered occasional pain in the fibroid owing to degenerative changes.

By 19th May (36 weeks), the patient had become generally uncomfortable, and the anus prolapsed, causing great distress and pain, so labour was induced by artificially rupturing the membranes. The foetal head presented in the right occipito-anterior position. Thirty-six hours later she delivered herself of a living male child weighing 6 pounds. The first stage of labour was long owing to uterine inertia, but the giving of oestrogens appeared to encourage uterine contractions. The second stage lasted only 10 minutes and, 5 minutes after delivery of the baby, the placenta was expelled from the vagina without haemorrhage.

The patient had an uneventful lying-in, and was discharged in a satisfactory condition with her breast-fed baby 21 days later. Only the haemorrhoids remained to cause any discomfort whatsoever After delivery the varicosities decreased as shown by the infra-red photographs taken 20 days (Figs. 3 and 4), and 15 weeks (Figs. 5 and 6) after delivery.

Upon re-examination at the time of the last photograph, the patient stated that she felt very well now, but that weakness had been marked during the first few weeks after leaving hospital. She thought that she now became more easily tired.

In general appearance she looked well and walked smartly without any disability. Examination of the legs revealed only mild varicosity and slight oedema of the right leg.

When questioned about her hours and times of duty in the job to which she had returned, it was obvious that her endurance exceeded that of many perfectly fit people of her age.

Review of the Literature.

In reviewing the literature on obstruction of the inferior vena cava, it is surprising to find that so large a vessel can be obstructed and yet the victim survive and subsequently show so little disability.

The factors which influence the prognosis appear to depend upon 3 conditions: (1) whether it is a surgical ligation, or whether the obstruction is a thrombosis secondary to some neoplastic or inflammatory condition; (2) whether the renal veins are thrombosed, and if so, whether by a gradual process or suddenly; and (3) the age of the patient.

Wakefield and Mayo (1934) reported a very interesting survey of cases collected from the Mayo Clinic, in which obstruction of the inferior vena cava had been found in the postmortem room, or diagnosed in the clinics, and supplemented their series with 19 cases of surgical ligation from the literature. For purposes of diagnostic criteria, they compared the symptoms and signs of 9 patients from the clinics, in whom thrombosis was secondary to previous illness, with those of 19 who were reported to have had a surgical ligation. They found in the

former series of 9 that a visible collateral circulation developed insidiously in all cases in the abdomen and legs, cyanosis of the skin peripheral to the obstruction developed in 7, and oedema in about half of them. In the group of 19, all except one were ligated below the renal veins, visible collateral circulation did not develop in any case, and only 5 of the 15 cases who survived had persistent oedema of the legs. One of the 4 who died had had the ligation made above the right renal vein. The authors suggest that in cases of thrombosis of the inferior vena cava where large abdominal tumours are present or widespread intrapelvic inflammation causing extensive phlebitis, the deep collateral veins may not develop sufficiently, and in consequence a collateral circulation becomes visible and oedema develops. Gaston and Folsom (1945) reported 2 cases of surgical ligation at the level of the bifurcation of the aorta, and both completely recovered—one a woman aged 49, upon whom the ligation was performed because of phlebothrombosis of the lower legs, and who 4 months later showed no evidence of oedema or enlarged veins, and was able to perform light work. The other patient was a 71-year-old man with thrombosis of the left common iliac vein. The inferior vena cava was ligated at the same level. Pitting of the legs appeared a few hours post-operatively, but began to subside 36 hours later as long as the patient was confined to bed. Reappearance of oedema of the legs on the 12th day with ascites and albuminuria suggested that thrombosis had extended to the level of the renal vessels. Diuresis and subsidence of oedema and ascites followed the intravenous injection of diuretics, however, and subsequent studies of the venous pressure made in the arm and foot simultaneously showed a gradual fall in the venous pressure of the foot as the collateral circulation developed. Three months later minimal oedema of the left leg, and enlarged veins over the abdomen and chest were the only signs present. Pfaff (1926) reported a case of haemorrhage into an abdominal cyst from a ruptured inferior vena cava, due to trauma, in a woman aged 48 years. At laparotomy, 11 days later, he ligated the inferior vena cava, and the patient made a good recovery.

Del Pino and Masciotra of Buenos Aires reported in 1929 a case of surgical ligation below the renal veins, because of injury during removal of a right-sided hydronephrosis in a patient 7 months pregnant. Neither cyanosis nor "chilling" developed in the lower extremities, which were carefully watched after the operation, but some oedema appeared in the right leg on the 8th day and lasted for 2 weeks, although the authors did not think that this was due to the ligation. Unfortunately she went into spontaneous premature labour on the day following the operation, and delivered herself of a live child, who lived 12 hours. The mother made a complete recovery, and only the loss of the baby marred the success of the case.

Fitzgerald (1943) also reported a case, in a man aged 31 years, of thrombosis of the inferior vena cava, spreading from a thrombosed left femoral vein, developed through trauma in lifting a heavy weight 9 years previously. True to the observations made in the 9 cases diagnosed in the Mayo Clinic and reported by Wakefield and Mayo, this man showed marked abdominal collateral circulation and oedema of both legs. According to the report, when last seen, "he felt quite well".

Osler and McCrae (1927) state that thrombosis of a renal vein can occur without any marked symptoms—pain and tenderness in the kidney region, albuminuria, scanty excretion of urine, etc.—provided it develops gradually. This certainly

agrees with the description given by Keen (1940) who found thrombosis of the inferior vena cava in a dissecting-room body: this subject had been an inmate of the infirmary for the last 11 years of his life, yet varicosity of the right leg was the only clinical abnormality ever observed, and this had been disregarded, as he walked without complaint. Keen states that the renal veins were thrombosed, and in view of the perfect collateral circulation draining the kidneys, he suggests that the thrombosis must have begun low in the inferior vena cava early in life, and that the gradual encroachment on the renal veins by the thrombosis was counterbalanced by the youthful resiliency of the venous system in developing an efficient collateral circulation.

Surgical ligation of the inferior vena cava above the renal veins, however, is reputed to have been successfully performed in 1902 by Turpesa in 3 cases out of 4. Gosset and Lecene, 2 years later, similarly ligated the inferior vena cava, but their patient died. Thereupon they initiated a series of experiments with dogs. They found that death occurred invariably when the inferior vena cava was ligated above the renal vein. Leotta in 1907 confirmed these experiments. Bejan and Cohn in 1911 pursued this research in animals further by placing the ligature between the renal and suprarenal veins. The 5 animals so treated all survived, but 4 others in whom the ligature was placed above the suprarenal veins, all died. Addis and Lew (1939) were also interested in the significance of thrombosis of the renal veins, and as a result of experiments with rats of various ages, they found that when they tied the inferior vena cava above the level of the renal veins, the survival incidence was proportional to age—the younger the rat, the greater were its chances of survival.

It is difficult to estimate to what extent these experiments may claim to be applicable to human beings, but all surgeons who have reported cases within recent years stress that their ligatures were applied below the level of the renal veins, and attribute their success to this. Of the 19 surgical ligatures quoted by Wakefield and Mayo, in only 1 instance was the ligature made (by necessity) above the right renal vein, and it would appear certain that this sudden occlusion was the cause of death.

A series of physiological experiments and observations were carried out by Burch and Winsor (1943) on 5 patients (aged 21, 21, 27, 31 and 67) following ligation of the inferior vena cava for therapeutic reasons, between 8 and 18 days after surgical operations. They emphasized that ligation had been performed below the renal veins, and little discomfort had been experienced by the patients. In one observation series, they recorded the venous pressure in the feet, compared it with that in the arm and found that it was markedly raised in all cases, but gradually fell as the collateral circulation developed. Re-examination 10 months later showed that the pressure had not returned to normal, although the oedema had disappeared in the legs of 3 of them: it did persist, however, in the 67-year-old patient. (The fifth patient had died in the meantime—cause unknown.) In the light of Addis and Lew's experiments, and Keen's remarks, it was only to be expected that the 67-year-old patient would exhibit evidence of difficulty in establishing a collateral circulation. Similarly, this might well be the explanation of the visible collateral veins, which developed after surgical ligation of the inferior vena cava in the 71-year-old patient reported by Gaston and Folsom.

The anatomy of the collateral circulation in thrombosis of the inferior vena cava has been described in detail by Keen, after dissection of the body in which this con-

dition was discovered in the dissecting room. The thrombosis extended from the common iliac veins to the groove in the liver, where the hepatic veins join the inferior vena cava. He found that the kidneys were drained mostly by dilatation of numerous peri-nephric veins, which on the right drained into a dilated sub-costal vein, and on the left into the inferior hemi-azygos vein. The pelvic organs (excluding the rectum) were drained partly by a large vein accompanying each ureter to the supra-renal plexus, and partly on the right side, with the veins of the right lower limb, by fresh anastomotic channels opened up in the direction of the deep circumflex iliac and ilio-lumbar veins. The right leg showed considerable varicosity, but there was none in the left leg, which drained *via* a patent common iliac vein to an azygos vein running behind the inferior vena cava to the dilated sub-costal vein.

Conclusion.

This case not only supports the findings of other observers in that the inferior vena cava can be permanently obstructed and yet the patient recover and live a moderately active life, but it also demonstrates that such a patient of child-bearing age can conceive and ultimately give birth by spontaneous delivery to a live child, and even suffer no apparent physical deterioration.

I have pleasure in thanking Professor James Young for his permission and encouragement to publish this case; Mr. M. R. Ewing, F.R.C.S., of the Department of Surgery, for collaboration; Mr. E. V. Willmott, F.R.P.S., and Mr. E. A. Sheppard for the infra-red photography; and my wife, Mary M. C. Foulkes, M.A., for translation of foreign literature.

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FIG. 1.
At 24-weeks' gestation.

FIG. 2.
At 24-weeks' gestation.

FIG. 3.
Twenty days after delivery.

FIG. 4.
Twenty days after delivery.

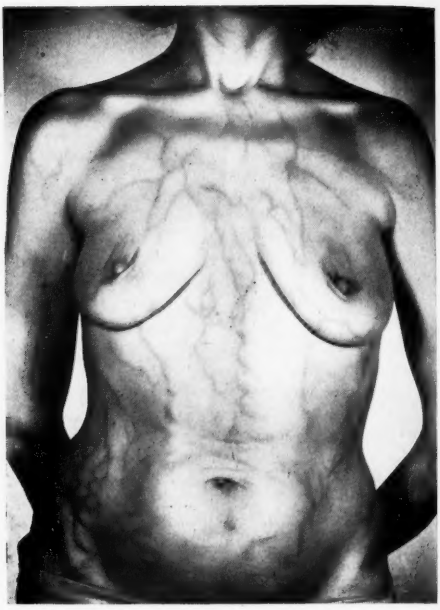

FIG. 5.
Fifteen weeks after delivery.

FIG. 6.
Fifteen weeks after delivery.

DYSGERMINOMA OVARII
(Report of a Case)

BY

H. SOBHI, M.B., D.G.O., F.R.C.S.,

AND

H. K. TOPPOZADA, M.S., L.M., D.G.O.,

From the Department of Gynaecology and Obstetrics of the Faculty of Medicine, Farouk I University, Alexandria, Egypt.

THE patient was admitted on 13th March, 1945. She was a 20-year-old woman, who had been married 5 months. Her menstrual history was normal and she had never been pregnant. She complained of a mass in the abdomen, which she first noticed soon after marriage. It started low down; later, as it increased rapidly in size and almost filled the whole abdomen, the patient had become short of breath on slight exertion.

On examination her general condition was moderate, pulse 98; blood-pressure, 140/90; the blood picture was normal and the urine contained a trace of albumen, although the urea clearance test and blood non-protein nitrogen were normal. The secondary sexual characters were normal.

The abdomen, although much distended, moved with respiration; there was a bossed mass arising from the pelvis, and reaching up to 2 fingers' breadth below the xiphisternum. It mainly filled the left side of the abdomen, and also encroached on and occupied most of the right side. Its consistency was generally hard. It had a limited amount of mobility from side to side, but not from above downwards. There was no tenderness, and shifting dullness could not be detected. The left loin was partly filled by the tumour.

On vaginal examination a conical cervix was found pulled high up and in to the right side of the pelvis. The body of the uterus was undersized, fixed to the lower part of the tumour, and sinistroflexed. There was a large, hard, irregular tumour filling the left and anterior segments of the pelvis and displacing the uterus posteriorly and to the left side.

A tentative preoperative diagnosis of dysgerminoma of the ovary was made by the junior author. The grounds for this diagnosis were: the age of the patient, the hypoplastic uterus, the rapid growth of the solid tumour, the absence of ascites or other frankly malignant clinical signs, and the absence of menstrual disturbances or other hormonal effects. Although no dysgerminoma of this size had been reported previously, the reasons stated above induced us to take this as our first diagnosis.

Operation. The senior author (assisted by H. K. T.) explored the abdomen on 27th March, 1945. The tumour was found arising from the left ovary; the greater omentum, the descending colon, and the anterior abdominal wall were adherent to the tumour, and the adhesions contained large dilated veins. Moreover, the tumour was densely adherent to the left broad ligament and to the hypoplastic uterus.

After severing the adhesions, the tumour was removed with the uterus and both adnexae. No palpable lymph glands were found.

The patient had an uninterrupted recovery and left the hospital in good condition on 22nd April, 1945. She was sent after discharge to the Radiological Department of the University Hospital, where she received deep irradiation therapy of the pelvis. She was last seen on 23rd February, 1948; no abnormality could be detected on examination, and amenorrhoea was her only complaint.

Pathological report. The tumour sent was 20 × 14 × 25 cm., and hard in consistency except in some small areas near the anterior surface, where it was soft. Many dilated veins were present in its capsule and showing on the surface. The uterus was adherent to its lower pole and was hypoplastic. The Fallopian tubes and right ovary showed no abnormality.

On microscopic examination the tumour was found composed of diffuse sheets of large round cells with large vesicular nuclei. Some mitotic figures were seen, though anaplasia was not marked (Fig. 1). The tumour cells were surrounded by a loose oedematous connective tissue stroma which was densely infiltrated with lymphocytes.

Diagnosis. Dysgerminoma of the left ovary.

Discussion.

Dysgerminoma of the ovary is a rare ovarian neoplasm; it is a "neuter" dysontogenetic tumour (Novak, 1946; Spencer and Reel, 1947) which is found in the ovary, testicle or hermaphroditic gonad (Barzilai, 1943; Novak, 1946; Meyer, 1931b; Greenblatt and Pund, 1938). Schiller (1934) reported a dysgerminoma of the uterus; he believed that extraovarian dysgerminomata may be due to simultaneous anaplastic growth in anlagen of indifferent gonadal tissue left over from early embryonic life at various points along the Müllerian duct. But Novak, Meyer, and many others have disputed this possibility, and have attributed the presence of extraovarian dysgerminomata to malignant spread from a primary ovarian lesion (Novak and Gray, 1938).

This tumour has been given many obsolete names; one of these, given to it by Chevassu, still obtains in French literature, i.e., seminoma (Novak, 1946). Kleine (1934) called it "large-cell carcinoma" (Grosszelliges Karzinom). Robert Meyer (1930, 1931a, 1931b) gave it the well-recognized and time-honoured name "dysgerminoma ovarii", and condemned the term seminoma, which conveyed an erroneous impression about its origin. According to this pathologist, the tumour arises from rests of mesenchymal cells of the early sexually undifferentiated gonad, i.e., before its development into an ovary or testicle (Barzilai, 1943; Novak, 1946; Meyer, 1931a; Novak and Gray, 1938). In an embryo 7 weeks old or less, it cannot be certain to which sex the gonad is to be assigned (Keith, 1913), and its cells may give origin to a dysgerminoma if they persist into extrauterine life (Russell, 1938). That is why this tumour is found in the testicle as well as in the ovary; it has also been found in the ovotestis of a true hermaphrodite (Novak, 1946). On the other hand, Giest (1942) postulates that it arises from certain cells of the surface epithelium of the anlage of the ovary; Meigs (1934) believes that it may result from a one-sided development of a teratoma. Teilum (1946) recently classified it as one type of "gonocytoma"—a group of tumours arising from a particular testicular anlage in the ovary (the medullary cords). Others consider it a special type of sarcoma, as it is a malignant neoplasm of the mesenchymal tissue of the

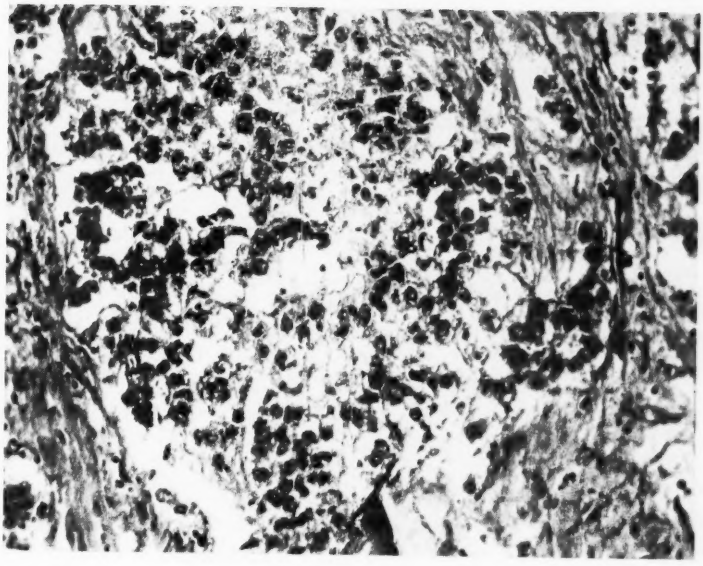

FIG. 1.

Showing the diffuse pattern of dysgerminoma ovarii. Lymphocytes are seen in the connective-tissue stroma at the sides. × 440

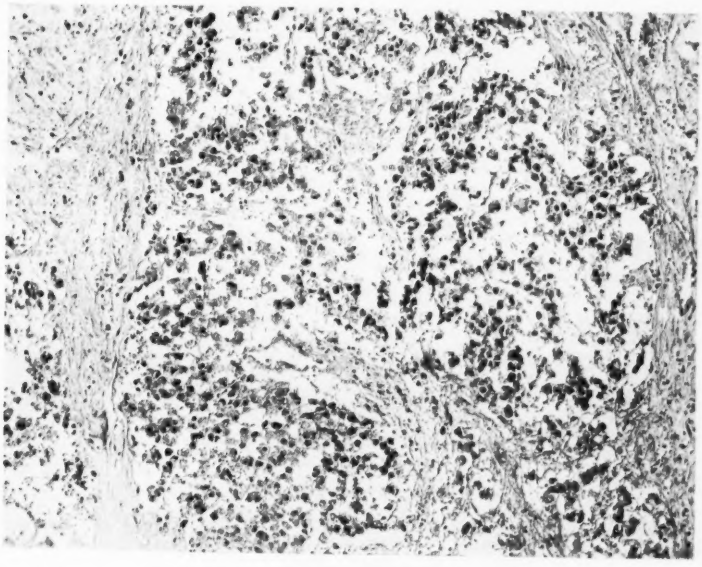

FIG. 2.

Showing an atypical alveolar pattern. × 120

H.S.& H.K.T.

ovary (Barzilai, 1943; Spencer and Reel, 1947); as a matter of fact, many cases have been formerly misinterpreted as sarcomata (Gittins and Hawksley, 1932).

The gross characteristics of this tumour are not pathognomonic; it may be bilateral (Barzilai, 1943; Bourne, 1945; Long, Ziskind and Storck, 1941; Chaney and Greenblatt, 1938; Schiller, 1936) or unilateral (Novak, 1946; Dockerty, 1942; Peel, 1943; Giest and Spielman, 1943). Its size can be as small as a plum or as big as a large water-melon, practically filling the abdomen (Marek and Phillips, 1947); the largest specimen reported up to 1938 was 25 × 17 × 15 cm. (Russell, 1938). The tumour is usually rounded and knobby, though the surface is smooth; it is typically "rubbery" in consistency, but large tumours with secondary changes may be spongy and friable. It is surrounded by a fibrous capsule that remains intact until the advanced malignant stage, when it gets invaded by the tumour tissue and the surface becomes fixed by adhesions to the neighbouring structures. There are at least two recorded specimens with torsion of the pedicle (Novak, 1946; Klein, 1934). Ascites may be associated with it (Novak, 1946; Russell, 1938). The cut surface is greyish pink, homogenous and brain-like. Necrotic areas and interstitial haemorrhages are commonly seen in large tumours; cystic spaces are infrequent and small.

The microscopic picture is characteristic; the tumour is made up of parenchyma-cells arranged in patterns that are surrounded by connective-tissue stroma. The tumour cells are very fragile and need special preparation of the specimens; classically they are uniform, large, polyhedral cells with well-demarcated cell boundaries. The cytoplasm is abundant, granular, eosinophilic, and rich in glycogen. The nuclei are central, large, and round; each nucleus contains 2 or 3 nucleoli. Mitotic figures are frequently seen. The sections give a feeble fat-staining reaction. The cytoplasm tends to dissolve in paraffin sections, leaving a collapsed cell-outline and a vacuolated interior (from the lipoid nature of the cell contents) (Russell, 1938). If a specimen is fixed in formalin, the cytoplasm shrinks, leaving the nuclei packed together and the cells then resemble those of a round-cell sarcoma. This is probably why a dysgerminoma has repeatedly been mistaken for a sarcoma. The tumour cells are arranged in certain patterns; in the diffuse or medullary pattern (Fig. 1) the cells are found forming large sheets with interspersed thin connective tissue strands. In the columnar pattern the cells are arranged in single layers separated from each other by connective-tissue septa. In the alveolar pattern, the most common, there are groups or nests of tumour-cells surrounded by a connective-tissue stroma (Fig. 2). The connective-tissue varies in amount and is generally less near the centre of the tumour; more connective-tissue and less cellularity in any tumour indicate a lower grade of malignancy (Fauvet, 1934, 1936). The stroma is typically an oedematous fibrous tissue invaded by lymphocytes (Russell, 1938; Long, Ziskind and Storck, 1941); large horse-shoe giant-cells may also be present. That is why tuberculosis has been suspected in some reported tumours. The giant-cells are concerned with removal of lipoid material resulting from breaking down of the tumour (Schiller, 1936). Regressive changes are frequently seen near the centre of a tumour, e.g., haemorrhage, necrosis, and cystic degeneration (Schomaker, Glascock, and Chapman, 1947).

This tumour is undoubtedly malignant (Barzilai, 1943; Novak, 1946; Novak and Gray, 1938; Giest and Spielman, 1943; Föderl, 1938; Mazel, 1947); but some authorities still consider it a relatively

benign tumour (Russell, 1938; Bourne, 1945; Schiller, 1936; Crossen and Crossen, 1944; Greenhill, 1943; Schneider and Vesell, 1947). Döderlein (quoted by Novak, 1946) has found 25 per cent of 53 reported cases which he studied as having extrapelvic metastasis. Even those who believe in its relatively benign nature give this tumour a 5-year survival rate; this rate, though varying from 60 per cent (Greenhill, 1943) to 23 per cent (Föderl, 1938), still means that this tumour can be malignant if left long enough. It invades the neighbouring organs and later metastasises in the regional lymph glands (Barzilai, 1943; Novak, 1946), the omentum, the viscera, and the bones (Stoia, Stanciulescue and Cioc, 1939).

The tumour is "neuter", i.e., it has no sex hormone activity (Barzilai, 1943; Novak, 1946; Meyer, 1931a; Shaw, 1945; Spielman and Morton, 1938).

Numerous workers have demonstrated a gonadotrophic hormone in its extracts; excessive amounts of this hormone in the patient's urine can give a positive Aschheim-Zondek reaction (Barzilai, 1943; Russell, 1938; Giest and Spielman, 1943; Shaw, 1945; Spielman and Morton, 1938). Gough (1938) claims a masculinizing activity for this tumour; others believe that it may have an inhibitory influence on normal female physiology (Long, Ziskind and Storck, 1941). Both these views are dismissed by the majority of writers, who believe in its neutral nature.

It is a rare ovarian tumour, which is three times less frequent than the granulosa-cell tumour of the ovary, and it accounts for 3 per cent of all primary malignant ovarian tumours (Novak, 1946; Föderl, 1938).

Dysgerminoma of the ovary is found in young patients, while in the testicle it is rarely seen before the age of 40 (Schiller, 1936); 70 per cent of the females affected are under 20 years of age (Greenhill, 1943). The youngest case recorded was in a child 4 years old (Russell, 1938), and the oldest in a woman 52 years old (Fauvet, 1934, 1936). The tumour has been repeatedly removed during pregnancy, labour, and the puerperium (Novak, 1946; Russell, 1938; Schomaker, *et al.*, 1947; Schneider and Vesell, 1947; Nyst, 1940; Stabler and Thomson, 1937; Rojas, 1946; Abernethy, 1943; Falk and Bunkin, 1947). There were 300 cases reported up to April 1947 (Schneider and Vesell, 1947), of which Novak (1946) examined 17 and Föderl (1938) 13.

The most common age-group affected is between 10 and 20 years of age (Novak, 1946; Chaney and Greenblatt, 1938). It is commonly found in patients with underdeveloped genitalia; several reports were also published of cases seen in pseudohermaphrodites and in true hermaphrodites (Barzilai, 1943; Novak, 1946; Meyer, 1931a; Greenblatt and Pund, 1938; Long, Ziskind and Storck, 1941; Neumann, 1930). But it is definitely more commonly found in women with normal genitalia (Novak and Gray, 1938; Selye, 1946). Seegar (1938) studied 79 cases from the literature, without any evidence of true or pseudo-hermaphroditism. Clinically the tumour has no characteristic signs or symptoms; it is a rapidly-growing solid ovarian tumour, which may be unilateral or bilateral (Barzilai, 1943; Novak, 1946; Long, Ziskind and Storck, 1941; Föderl, 1938). It retains a certain amount of mobility in many cases; degeneration, though rare, may give rise to a febrile general reaction (Marek and Phillips, 1947), night sweats and leucocytosis (Long, Ziskind and Storck, 1941). Menstruation is not affected by the tumour. Otherwise a dysgerminoma gives the clinical picture of an ordinary solid ovarian tumour (benign or malignant). All cases reported in the literature were diagnosed only by the pathologist.

Some surgeons prefer conservative surgery in the treatment of these tumours (Giest and Spielman, 1943; Greenhill, 1943; Sailer, 1940); this is done when the tumour is unilateral, free of adhesions, has an intact capsule, and especially so if it is detected in a young girl. In these cases only the affected ovary is removed; the idea is to give the young patient a chance to become pregnant (Greenhill, 1943; Schneider and Vesell, 1947; Kleitman, 1946; Seegar, 1938). On the other hand, when a tumour is bilateral, adherent, or infiltrating it is considered malignant (Long, Ziskind and Storck, 1941; Dworzak, 1935), and radical surgery is advised—the tumour, the uterus, both adnexae, and if possible the infiltrated organ are all removed. Deep irradiation of the pelvic organs and the regional lymphglands is always indicated in these cases, as these tumours and their secondaries are very radiosensitive (Barzilai, 1943; Novak, 1946; Novak and Gray, 1938; Russell, 1938; Dockerty, 1942; Peel, 1943).

Conclusion.

A case is reported on account of its interesting features; the diagnosis was suggested before operation as the patient was young, and the tumour was solid and rapidly growing, and the uterus was hypoplastic. Furthermore, it showed no hormonal influences and it was not accompanied by ascites or other frank malignant clinical signs. It is probably the largest dysgerminoma so far recorded.

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ERRATUM

In the obituary of the late Dr. J. H. Willett, in the October issue of the Journal, the invention of the scalp forceps for placenta praevia was mistakenly attributed to him. The Editor is anxious that this wrong impression should be removed as soon as possible. The inventor was Dr. J. A. Willett.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A special meeting of the Council was held on Friday, 1st October, 1948, at the College House with the President, Sir William Gilliatt, in the chair.

The Honorary Fellowship of the College was conferred on Dr. Emil Novak, of Baltimore, U.S.A.

Allan Frederick Hollinrake, of Ontario, was admitted to the Fellowship of the College.

The following were admitted to the Membership of the College:

Ian Struan Robertson Bain.
Henrietta Elizabeth Banting.
Trevor Lewys Stanhope Baynes.
Samuel Behrman.
Douglas Charles Aitchison Bevis.
Charles Christopher Bowley.
Tristam St. Vincent William Buss.
Lloyd Woodrow Cox.
Mary Elizabeth Egerton.
Thomas Elliot Elliot.
Gilbert McIlwrick Forsyth.
Harold Derek Freeth.
George Taylor Gibson.
John Hartley Gibson.
Andrew Graham.
Alfred Henry Grenz.
Constance Amy Grey.
Harold Bickford Hattam.
Carl Clifford Henneberg.
Ebbie Hesselberg.
Dennis Woodfall Higson.
John Colgate Holman.
Kenneth Robert Hudson.
Alun Gareth Jones.
James Barclay Joyce.
William Thomas Kenny.
George Gladstone Kerster.
Robert Arthur Hugh Kinch.
Samuel Lask.
Thomas Loftus Townshend Lewis.
William Macfarlane.
Stephen Herbert Madden.
Helen Margaret Mayer.
Eiohn Lynn Forsyth McConnachie.
John Macdonald McKiddie.
Gordon William Heyes Millington.
Frank Lionel Edward Musgrove.
James Raymond Norris.
John Joseph Francis O'Sullivan.
Joseph Henry Patterson.
Anthony Cecil Pearson.
William Henry Peek.
Stanley Dreland Perchard.
David Prysor-Jones.
Edward Harford Rees.
Stanley McRae Reid.
Hujohn Armstrong Ripman.
Donald Norman Struan Robertson.
Basil Walter Sanderson.
George Alfred Silley.
Alan Ambery Smith.
Tom Smith.
George John Sophian.
Christine Margaret Stacey.
Patrick Christopher Steptoe.
Christopher Seymer Newton Swan.
Ralph Arnold Thatcher.
Gwyn Stuart Thomas.
Robert George Whitelaw.
Rhys Meyrick Williams.
Martin Sadler Williamson.
Harold Geoffrey Wolskel.
Peter Spence Wright.
Ratcliffe Bowen Wright.

THE TWELFTH BRITISH CONGRESS OF OBSTETRICS AND GYNAECOLOGY, 6th, 7th and 8th JULY, 1949

To be held in the Friends Meeting House, Euston Road, London, N.W.1.

President: SIR EARDLEY HOLLAND.

Hon. Secretaries: A. JOSEPH WRIGLEY and IAN JACKSON.

58 Queen Anne Street (Royal College of Obstetricians and Gynaecologists), London, W.1.

Wednesday, July 6th.

Morning Session, 10 a.m. (*Chairman*: THE PRESIDENT).
The Congress will be declared open by the Minister of Health.

"Modern Caesarean Section." Introduced by Mr. C. McIntosh Marshall (Liverpool).

Afternoon Session, 2.0 p.m. (*Chairman*: PROFESSOR HILDA LLOYD).

(1) **Guest Paper ("Endometriosis").** Dr. Joe Meigs (Boston, Mass.).

(2) **"The Methods of Assay and Clinical Significance of Pregnanediol in the Urine."** Introduced by Professor C. F. Marrian (Edinburgh) and Dr. G. I. M. Swyer (London).

8.45 p.m. Reception by the President and Council of the Royal College of Obstetricians and Gynaecologists at the University of London, Bloomsbury, W.C.1.

Thursday, July 7th.

Morning Session, 10.0 a.m. (*Chairman*: SIR WILLIAM GILLIATT).

"Essential Hypertension in Pregnancy." Introduced by Professor George W. Pickering (London) and Professor F. J. Browne (London).

Afternoon Session, 2.0 p.m. (*Chairman*: DR. JOHN HEWITT).

(1) **"The Management of Pregnancy in Diabetics."** Introduced by Mr. John H. Peel (London) and Dr. W. G. Oakley (London).

(2) **"Hernia of Pouch of Douglas."** Introduced by Mr. Charles D. Read (London).

8.0.–10.30 p.m. Reception by the President of the Congress at the Zoological Gardens by courtesy of the Council of the Zoological Society of London.

Friday, July 8th.

Morning Session, 10.0 a.m. (*Chairman*: PROFESSOR O'DONEL T. D. BROWNE).

"Modern Concepts in Diagnosis, Treatment and Prognosis of Carcinoma of the Uterus."

(1) **"The Diagnosis by Vaginal Smear."** Dr. J. E. Ayre (Montreal).

(2) **"Pre-Cancerous Cellular Changes in Carcinoma of the Cervix."** Professor Gilbert I. Strachan (Cardiff).

(3) **"Prognosis based on Biopsies."** Mr. Glucksmann (Cambridge).

(4) **"The Operation of Pelvic Exenteration."** Dr. Joe Meigs (Boston, Mass.).

A Discussion will follow each Paper.

Afternoon Session, 2.0 p.m. (*Chairman*: DR. E. CHALMERS FAHMY).

Discussion on Maternal Mortality. Introduced by Sir William Gilliatt (London).

7.45 p.m. Congress Banquet in Guildhall.

Owing to the difficulties that exist at the present time in arranging hotel accommodation, travel, etc., will all those who hope to attend please apply as soon as possible to A. J. Wrigley, F.R.C.O.G., Hon. Sec., 58 Queen Anne Street (Royal College of Obstetricians and Gynaecologists), London, W.1.

REVIEW OF CURRENT LITERATURE

The Journal is fortunate in being able to run this Review in conjunction with the Abstracting Service of the British Medical Association. All the abstracts of this service which cover obstetrical and gynaecological literature and literature on the new-born are at our disposal. The Review will, however, contain in addition abstracts and titles of articles which, though not of sufficient general interest for publcation in the monthly volumes published by the British Medical Association, are yet sufficiently important for a specialist journal. It is to be hoped that our readers will collaborate in the preparation of these abstracts. Those who are willing to take part in the service are invited to communicate with the Editor, The Abstracting Service, B.M.A. House, Tavistock Square, London, W.C.1. There is special need of abstracters in foreign languages, and when offering his or her services the writer should indicate the language (apart from English) in which he or she is proficient. The name of the abstracter will be acknowledged in the text and payment will be made at the rate of ten shillings per abstract for English articles and twelve shillings and sixpence per abstract for articles from foreign languages.

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ANATOMY.

1786. **The Visceral Endopelvic Fascia and the Hypogastric Sheath.**

By E. UHLENHUTH, E. C. DAY, R. D. SMITH, and E. B. MIDDLETON. *Surg. Gynec. Obstet.*, **86**, 9–28, Jan. 1948. 11 figs., 17 refs.

The authors believe that a detailed knowledge of the visceral endopelvic fascia is valuable because: (1) The fascia provides a sheath or capsule for each of the pelvic viscera. (2) To this sheath are attached the supporting ligaments and other structures. (3) In the substance of this sheath lie the collecting lymph channels from viscera. In the form of perivascular sheaths it serves to fix and to render obvious the position of important vessels and nerves, and to divide the subperitoneal part of the pelvic cavity into distinct fascial compartments.

The authors accept Testut's definition and description of the parietal pelvic fascia but, believing that he overlooked important elements of the visceral fascia, they present a new account of the latter, based almost entirely on the dissection of a single embalmed pelvis of a coloured woman aged 29 years. They recognize the following subdivisions of the visceral pelvic fascia: (1) the fascial capsules of the pelvic viscera, (2) the fascia endopelvina, (3) the umbilical sheath, (4) the superior haemorrhoidal sheath, (5) the hypogastric sheath, (6) the recto-vesical (recto-vaginal) sheath, and (7) the loose areolar tissue. They claim originality for their descriptions of the hypogastric sheath and of the supporting mechanisms of the uterus, which they believe to be much more complex and important than would appear from former accounts.

The hypogastric root arises as two stout membranous layers which, springing from the parietal pelvic fascia, enclose the anterior division of the internal iliac vessels and the ureter. These layers pass forward towards the bladder and split into a superior hypogastric wing, an inferior hypogastric wing, and a presacral wing. The presacral wing passes across the front of the sacrum (splitting to enclose the rectum) and joins its fellow of the opposite side, thus shutting off from the rest of the pelvis a retrorectal space. The superior hypogastric wing splits at the lateral margin of the superior surface of the bladder to clothe the superior and infero-lateral surfaces of this organ. Laterally, it forms a roof for the space of Retzius, carrying the obliterated umbilical and superior vesical arteries in its substance, and extends over the brim of the pelvis to form a sheath for the external iliac vessels. The inferior hypogastric wing, as it extends medially, ventrally, and caudally from the hypogastric sheath, contains the ureter and the inferior vesical vessels. It is attached medially to the dorsolateral border of the bladder and laterally to the fascia endopelvina. This latter forms a horizontal sheet, springing from the fascia covering the upper surface of the levator ani and extending medially towards the bladder. It is attached to the latter only indirectly, however, through its connexion with the inferior hypogastric wing. It forms the floor of the space of Retzius.

The so-called ligament of Mackenrodt is nothing but this inferior hypogastric wing, and plays no part in the support of the uterus, but is concerned with the fixation of the bladder. The uterus is fixed by the attachment to its cervix of a special slip of levator ani (named by the authors the portio cardinalis of the levator ani), which opposes the tendency of the uterus to exert medial traction on the "ligament of Mackenrodt", and thus on the uterine vessels. If this slip should be damaged the drag of the uterus on the vessels may be sufficient to cause obstruction of the ureter at the point where it is crossed by the vessels, since the ureter is fixed in position by the fascia of the inferior hypogastric wing and cannot yield to the pull of the vessels. It is suggested that the hydronephrosis associated with prolapse of the uterus may be relieved by ligation and division of the uterine vessels, the ovarian vessels then maintaining the blood supply of the uterus.

The rectum and retrorectal space may be easily reached through the space of Retzius without opening the peritoneum. This space is separated from the retrorectal space by thin fascia only, below the level of the inferior vesical artery. *H. Hughes*

1787. **The Rectogenital Septum.**

By E. UHLENHUTH, W. M. WOLFE, E. M. SMITH, and E. B. MIDDLETON. *Surg. Gynec. Obstet.*, **86**, 148–163, Feb. 1948. 14 figs., 7 refs.

The authors, working in the University of Maryland Medical School, Baltimore, demonstrate that the "rectogenital septum", denoting the male rectovesical septum and the female rectovaginal septum collectively, is of pertioneal origin and not a purely fascial structure. Cuneo and Veau in 1899 advanced the view that the prostato-peritoneal fascia was a peritoneal derivative, but in 1922 Wesson claimed that the rectovesical fascia is of fascial nature. Other investigators have failed to demonstrate a septum in the female, stating that the tissue between rectum and vagina is but the fascial capsule of the two organs with "loose areolar tissue between".

The authors' investigations were made on 37 male and female infants, 26 adult male cadavers, and a small number of female cadavers. [Beautiful illustrations of dissections, 5 in the male and 5 in the female, are reproduced.] The dissections offer convincing proof that a peritoneal pouch usually exists in the foetus down to the pelvic floor, and that the walls of the pouch fuse at or near term. Measurements of the distance in adults from the bottom of the rectovesical pouch to the anterior anal commissure showed large variations in both male and female (rectovaginal), being on an average much smaller in the female. In the male the septum was always separated from the rectum

by loose connective tissue and more closely adherent to the bladder and seminal vesicles. In one case it was not found at all, and this was explained by the exceptionally cranial situation of the recto-vesical pouch (110 mm. from the ventral commissure of the anus). The surface of the septum was generally firm, glistening, and greenish, whereas adjacent fascial membranes were dull, whitish and felt-like. The configuration of the peritoneum at the caudal end of the pouch where the septum began was often seen as a white scar line. In infants the septum could be split and the pouch "re-opened" even to the floor of the pelvis.

[The views expressed and the findings appear to coincide with those of Kirk (*Proc. R. Soc. Med.*, 1947, **40**, 876), who stated: "The urorectal septum is at first solid mesoderm but later becomes excavated by an extension into it of the coelomic (peritoneal) cavity. . . . In the male at birth the rectovesical pouch extends to the perineal body. . . . Later . . . (it) is obliterated by adhesions of its walls."] *Elliot E. Philipp.*

PHYSIOLOGY.

1788. **Study of the Temperature of the Cervix Uteri.** (Etude sur la température cervico-utérine.)

By A. NETTER. *Presse méd.*, **56**, 506–507, July 17, 1948. 1 fig., 1 ref.

1789. **Inhibitory Action of Homologous Liver Extract on Oestrus in the Rat.** (Azione inibitrice dell' estratto epatico omologo sull'estro del ratto.)

By R. CANDIDO and M. GERLI. *Arch. Ostet. Ginec.*, **53**, 105–119, Mar.–Apr. 1948. 14 figs., 12 refs.

These investigations, carried out at the Obstetrical and Gynaecological Clinic of the University of Naples, are based on a theory propounded by Zondek in 1934 that folliculin may be metabolized by the liver, and on experiments by various authors which showed that natural and synthetic oestrogens are inactivated by liver extracts *in vitro*.

Varying amounts of watery extracts from livers of mature rats were injected into 27 female rats whose sexual cycle had previously been typed by examination of their vaginal smears. Daily injections of 2 ml. of the extract for 10 consecutive days resulted, in the majority of animals so treated, in persistence of di-oestrus with suppression of the oestrus cycle. Smaller doses caused prolongation of di-oestrus only or no modification of the cycle. Histologically intense and widespread luteinization with extreme scarcity or complete absence of developing follicles was constantly demonstrated in the ovaries. The vagina was in quiescent state; the uterine cornua were small and atrophic. The hypophysis and the liver were practically unchanged.

The authors offer two possible explanations for these phenomena. Either the liver extracts contained a luteinizing factor and the massive luteinization of the ovaries arrested ripening of follicles and therefore the vaginal cycle, or the extracts neutralized or inactivated the natural oestrogens, causing hypofolliculinaemia and, through the action of the hypophysis, overproduction of luteinizing, and relative underproduction of follicle-stimulating, gonadotrophin and thus suppression of the oestrous cycle. *N. Alders*

1790. **Studies on the Human Corpus Luteum. Histologic Variations in Corpora Lutea and in Corpus Luteum—Endometrial Relationships at the Onset of Normal Menstruation.**

By J. I. BREWER and H. O. JONES. *Amer. J. Obstet. Gynec.*, **54**, 561–575, Oct. 1947. 12 figs., 5 refs.

A study was made of the variations in the life cycle of the human corpus luteum, the endometrial cycle, and the relation between the two. The material on which the study was based consisted of 10 uteri, each together with a corpus luteum, removed from patients aged 23 to 47. Seven of the uteri were removed on the first day of menstruation and 2 before the onset of menstruation. The menstrual cycle had been normal in each case. Degeneration of the granulosa lutein cells first takes place some 4 to 6 days before the onset of menstruation. The degeneration is slowly progressive and can be reversed by the onset of pregnancy. It may involve all the cells or only local groups, and occasionally may be almost absent at the onset of menstruation. In view of these differences it was concluded that there are considerable variations in the granulosa lutein cells before and immediately after the onset of menstruation. Similarly, in the study of the endometrial patterns it was observed that considerable variations occurred which could not be correlated with the histological activity of the corpus luteum. In one specimen, in spite of an apparently normal corpus luteum, the endometrium showed the changes that are characteristic of anovulatory menstruation.

From these findings the authors concluded that study of endometrial specimens removed at or near the time of menstruation may lead to an erroneous interpretation of corpus luteum activity.

J. Stallworthy

1791. **Serum Iron in Normal Women.**

By S. DAHL. *Brit. med. J.*, **1**, 731–733, Apr. 17, 1948. 1 fig., 10 refs.

Serum iron values in healthy women ranged from 68 to 194 μg., most lying between 70 and 140 μg. per 100 ml. The concentration was lower in menstruating women than in those not menstruating.

Douglas H. Collins

1792. **The First Menstrual Period After Labour and Abortion.** (Erste Menstruation nach Partus und Abortus.)

By P. ELSNER. *Wien. klin. Wschr.*, **60**, 433–435, July 9, 1948. 2 figs., 18 refs.

1793. **"Substance P" in Menstruation.** (A proposito della S.P. nella mestruazione.)

By M. BERTANI. *Monit. ostet.-gynec.*, **19**, 92-102, Mar.-Apr., 1948. 36 refs.

1794. **A Comparative Study of Vaginal and Cervical Cornification in Human Subjects.**

By J. E. AYRE, P. M. CHEVALIER, and W. B. AYRE. *J. clin. Endocrinol.*, **7**, 749-752, Nov. 1947. 1 fig., 5 refs.

Cervical and vaginal smears covering all stages of the menstrual cycle in 125 patients with a wide range of ages were compared as regards the amount of cornification. Cervical smears were taken by means of a special speculum, the scraping being taken from the squamous margin of the squamo-columnar junction. The vaginal smears were taken by light scraping of the lateral wall of the vagina. The smears were stained with Papanicolaou's polychrome stain. The level of cornification was estimated by counting the number of cornified cells, large flat epithelial cells with pyknotic nuclei and acidophilic cytoplasm, per 100 squamous epithelial cells. Pseudocornified cells having acidophilic cytoplasm but no nuclear pyknosis were not included.

The cornification level in both smears varied with the phase of the cycle, rising gradually during the follicular phase to a peak (over 50 per cent) at ovulation and falling irregularly to a level approaching zero just before menstruation. After either administration or injection of oestrogen in castrated or menopausal women, the level rises from zero to that found in the normal cycle, the rise appearing a few days after starting treatment and being proportional to the administered dose. [No figures given.] The time interval is shorter when oestrogen is given in vaginal suppositories. In 88.8 per cent of the cases the count of cornified cells was higher in cervical than in vaginal smears, the difference varying from 5 to 55 per cent. In 7.2 per cent levels were equal and only in 4 per cent was the count higher in vaginal than in cervical smears, the difference varying from 5 to 10 per cent. The reasons for this difference are discussed; it may be due to a greater sensitivity of the cervical epithelium to oestrogen, or to a higher concentration of oestrogen in the cervix, or to a combined effect of both these factors. *S. A. Simpson*

1795. **Cytological Cycle of the Urinary Sediment and its Parallelism with the Vaginal Cycle.**

By E. B. DEL CASTILLO, J. ARGONZ, and C. G. MAININI. *J. clin. Endocrinol.*, **8**, 76-87, Jan. 1948. 16 figs., 8 refs.

Smears of cells found in urine are made by rubbing with a wire loop the inner surface of a filter paper after most of the first morning specimen has filtered through it. The moist smear is immediately fixed in alcohol-ether and stained for 3 minutes (Schorr, *Science*, 1941, **94**, 545.) To prove that cells found in the urine were not extraneous, a catheter was introduced for not more than 1 cm. into the urethra for direct sampling of the urethral contents. After studying a group of cases, which included a normal prepuberal girl, normal adult women, menopausal women, patients with primary amenorrhoea and under oestrogen therapy, by both the urinary-cell and the vaginal-smear method, the authors maintain that there is close correlation in the morphology of the cells obtained from each source. *Magnus Haines*

1796. **A Comparison of Oral and Vaginal Epithelial Smears.**

By D. E. ZISKIN and R. MOULTON. *J. clin. Endocrinol.*, **8**, 146-165, Feb. 1948. 25 figs., 19 refs.

The work of Papanicolaou showed that it is possible to follow cyclical hormonal changes in the human female by daily observation of vaginal smears. An attempt is made in this article to correlate changes in the oral mucosa with those occurring in the vagina, in order to develop a simpler technique for following endocrine changes. In experiments on rhesus monkeys, administration of oestrogen was found to produce gingival hypertrophy and hyperkeratinization of the oral mucous membrane, whatever the endocrine status of the animal (normal, castrated, immature, or hypophysectomized); atrophy of the mucous membrane and reduction in the layer of keratin was brought about by castration or hypophysectomy. In the presence of chorionic gonadotrophin or progesterone, keratinization was greatly diminished. Similar changes were found in the oral mucous membrane of human subjects suffering from endocrine disturbances or receiving oestrogen therapy. For instance, in a child of 7 with adrenal hyperplasia and pseudohermaphroditism normal keratinization was absent while hyperkeratinization was found in those receiving oestrogen therapy and also in a patient suffering from Addison's disease.

Oral and vaginal smears were taken simultaneously from 23 women, some normal and and some suffering from mild endocrine disturbances. From a comparative study of these smears it is concluded that although the oral and vaginal epithelium undergo parallel changes in degree of cornification during the menstrual cycle and under oestrogen therapy, slight hormonal changes are more easily recognized in the vaginal smear; the latter affords a better indication of the time of ovulation, so that in spite of its technical advantages the oral smear cannot replace the vaginal smear in hormone study. *Margaret Puxon*

1797. **Simple Approach to the Study of Vaginal Smears: I. Variations in the Normal Sexual Cycle.**

By R. G. BONIME. *Amer. Practit., Phila.*, **2**, 664-670, June 1948. 10 figs., 7 refs.

1798. **Rapid Determination of Urinary Pregnanediol. Method Suitable for Routine Clinical Use.**

By I. F. SOMMERVILLE, G. F. MARRIAN, and R. J. KELLAR. *Lancet*, **2**, 89–90, July 17, 1948. 13 refs.

1799. **Oestrogens and Temperature Regulation.** (Oestrogènes et régulation thermique.)

By M. ALBEAUX-FERNET, E. HOUSSET, and — BOULET-GERCOURT. *Ann. Endocrinol., Paris*, **9**, 131–135, 1948. 1 fig., 4 refs.

1800. **Metabolism of the Steroid Hormones—The Metabolism of Progesterone and Ethinyl Testosterone.**

By R. I. DORFMAN, E. ROSS, and R. A. SHIPLEY. *Endocrinology*, **42**, 77–80, Feb. 1948. 9 refs.

It has not been possible to demonstrate the conversion of ethinyl testosterone to pregnanediol-3 (α), 20 (α), or any other steroid either in men or in women suffering from secondary amenorrhoea when daily oral doses of 300 mg. of the steroid were administered. Progesterone absorption from the gastro-intestinal tract was demonstrated by the isolation of sodium pregnanediol glucuronide after the administration of the progestational hormone. However, it was shown that the preganediol complex isolated by the Venning procedure contained a small amount of pregnanol-3 (α)-one-20 in addition to pregnanediol-3 (α), 20 (α). Thus it appears that pregnanol-3 (α)-one-20 can be classed as a metabolite of progesterone along with pregnanediol-3 (α), 20 (α).—[Authors' summary.]

1801. **The Effects of Progesterone, Oestradiol, Thyroid Hormone, and Androsterone on the Artificial Premature "Climacteric" of Pure Gonadal Origin Produced by Ovariectomy in Rats.**

By V. KORENCHEVSKY and V. E. JONES. *J. Gerontol.*, **3**, 21–39, Jan. 1948. 26 figs., 26 refs.

This is the fourth article of a series dealing with the action of female sex hormones. The work was done in the Gerontological Research Unit, Oxford, 78 ovariectomized rats being used for 3 experiments (14 as controls, 64 receiving hormones). The methods of administration and of estimation of results have been described in previous papers. importance was attached to the relative weights of organs per unit of fat-free body weight.

This work confirmed previous findings in many respects. There was slight gain in body weight and fat deposition after androsterone, and a decrease after thyroid and oestradiol, the depressing effect of which was not counteracted by androsterone and progesterone. It appears that for the greatest development of progestational changes in the uterus all four hormones are necessary. In contrast to uterine changes, in the vagina the greatest degree of mucification was observed in rats injected only with progesterone and oestradiol. The liver increased significantly in weight only after the simultaneous use of thyroid and oestradiol benzyl benzoate, while the simultaneous administration of all four hormones caused liver hypertrophy without much change in structure. In the case of the thyroid gland, the depressing effect of thyroid hormone outweighs the stimulating effect of a combination of androsterone and progesterone. Preputial glands hypertrophied only after androsterone.

The authors discuss the effects of oestrogens on the hypophysis in great detail, and review the work of others in this field. The present experiments emphasize the neutralizing effect of androsterone on oestrogenic hypertrophy of this organ, and also its involutionary effect on the thymus. The thyroid hormone was shown to be the main factor responsible for splenic hypertrophy; thyroid and androsterone caused cardiac hypertrophy.

Morag L. Insley

PREGNANCY.

1802. **Young and Elderly Primiparae.** (Primiparas jovens e primiparas idosas.)

By A. NOVIS. *Rev. brasil. Cir.*, **17**, 65–70, May 1948. 8 refs.

1803. **Can Menstruation Persist during Pregnancy?** (La menstruation peut-elle persister au cours de la grossesse?)

By P. MAGNIN and A. BURNOD. *Rev. franç. Gynéc.*, **43**, 235–248, June 1948. 34 refs.

1804. **A New Apparatus for Radiological Pelvimetry.** (Un nouvel appareil de radiopelvimétrie.)

By —. TRILLAT and —. MAGNIN. *Gynéc. et Obstét.*, **47**, 193–203, 1948. 5 figs.

The authors have applied to the Fabre method of radiopelvimetry the superimpression technique advocated by Thoms and Turpin in the U.S.A. With the American apparatus films are exposed with the patient in a half-sitting position, so that the inlet plane is parallel to the film on which the patient sits. The X-ray tube is centred at right angles to the inlet plane. After a first exposure, the patient is removed, tube and film remaining in place; the patient's place is taken by a leaden screen perforated by holes 1 cm. apart, and the film is again exposed. The present authors expose films with the patient lying on her abdomen, a position which, according to Portes and Blanche, is well tolerated by pregnant women. This position gives maximum visibility of the promontory and an excellent picture of the foetal head. The plane of the innominate lines (" transverse-pubic plane "), corresponding to the major part of the inlet plane, passing through the superior fourth of the pubis and the lateral dimples of Michaelis's lozenge, is marked by means of two lateral rulers, one on each side of the patient; the X-ray tube is above and behind the sacral region. The patient's place is afterwards taken by a metallic screen with punctate perforations 1 cm. apart which slides between the

fixed rulers. By this method the transverse diameter is measured exactly, but there are variations in the antero-posterior diameter, since the promontory overlaps the innominate lines.

The new method permits a double superimpression. The first superimpression is in the plane of the innominate lines, the transverso-pubic plane; the second superimpression is in the promonto-pubic plane, the other end of the same metallic screen being used. To avoid confusion with the first superimpression picture, this end has linear perforations.

After a technical description of the construction of the apparatus (mainly a swivelling ruler-frame for the metallic screen), the authors recapitulate the four main stages in the technique: (1) Markings are made on the patient at the union of the superior fourth and inferior three-fourths of the pubis, at the lateral dimples of Michaelis's lozenge, and above the spine of the fourth lumbar vertebra. (2) The patient lies on her abdomen between the two rulers of the mobile frame, and the angulation is noted when the frame inclination corresponds to the two pelvic planes under consideration. The first exposure is made. (3) The first superimpression picture is taken. (4) The second superimpression picture is taken, the end of the screen with linear perforations being placed in the inclination corresponding to the promonto-pubic plane. The linear markings on the film give the antero-posterior diameter, the punctate markings the transverse diameter.

[The posterior marking of the promonto-pubic plane (L4) is variable, but even a 2-cm. error will not result in an error greater than 2 mm. in the estimated antero-posterior diameter. It may prove difficult to assess correctly the contour of the promontory on these films, especially with foetal head interposition. An advantage of the method, mainly an advantage of the ventral position, is that the possible adaptation of the foetal head to the pelvic inlet is shown.] *H. Godar*

1805. **Radiological Pelvimetry with the Pelvic Inlet not Parallel to the Plate.** (Die röntgenologische Grössenbestimmung der Beckendurchmesser bei nicht platten-paralleler Beckeneingangsebene.)

By L. PREISSL. *Klin. Med., Wien*, **3**, 543–554, July 15, 1948. 6 figs.

1806. **A Simplified Method of Roentgen Pelvicephalometry.**

By A. K. WILSON. *Amer. J. Roentgenol.*, **59**, 688–698, May 1948. 5 figs., 4 refs.

1807. **Relaxin Content of Blood, Urine and Other Tissues of Pregnant and Postpartum Guinea Pigs.**

By M. X. ZARROW. *Proc. Soc. exp. Biol., N.Y.*, **66**, 488–491, Nov. 1947. 1 fig., 9 refs.

Relaxin, first detected in the blood of pregnant rabbits and guinea-pigs and later in other mammals, may be assayed by its effect of pubic-bone separation.

Blood samples, obtained by cardiac puncture from guinea-pigs weighing 600 to 800 g. with dated pregnancies, were pooled in groups according to the duration of pregnancy. By pooling, a sufficient quantity was obtained for the determinations. Urine samples were collected for the 24 hours before the blood collection and dialyzed against running tap water. Placentae and uteri, obtained on the 56th and 63rd days of pregnancy, were ground up and extracted twice with 3 per cent hydrochloric acid. These extracts, kept at pH 0.5 in the cold, were adjusted to pH 7.0 with 10 per cent sodium hydroxide before injection. Groups of guinea-pigs were studied at 15, 21, 28, 35, 42, 49, 56, and 63 days after mating (57 in all) and at 2, 6, 24, and 48 hours postpartum (23 in all). Urine samples were collected 42, 56, and 63 days after the animals had been mated. Test animals were given 0.1 g. oestradiol daily for 3 days before use. For each sample a concentration was obtained which gave 67 per cent response. The method of assay was that of Abramowitz *et al.* (*Endocrinology*, 1944, **34**, 103.)

Relaxation of the symphysis pubis began from the 18th to the 25th day in a series of 20 guinea-pigs. This corresponds with the appearance of relaxin (up to 0.5 guinea-pig units per ml. of serum) in the blood of pregnant guinea-pigs. The highest level, which is maintained for about 4 weeks, begins to fall before parturition (it was 0.33 units on the 63rd day after mating). It is suggested that a similar ante-partum fall in the relaxin levels occurs in women. Other findings suggest that the fall in relaxin levels in serum and urine may be due to a decreased output by the placenta.

Magnus Haines

1808. **The Role of the Steroid Hormones in the Relaxation of the Symphysis Pubis of the Guinea Pig.**

By M. X. ZARROW. *Endocrinology*, **42**, 129–140, Feb. 1948. 1 fig., 41 refs.

Relaxation of the symphysis pubis of the guinea-pig may be produced by treatment with: (*a*) oestradiol, (*b*) oestradiol and progesterone, and (*c*) oestradiol and relaxin. In the castrated, hysterectomized guinea-pig progesterone is without effect, whereas in the presence of a uterus treatment with oestradiol and progesterone both shortens the time required for pelvic separation as compared with oestradiol treatment alone and results in the formation of endogenous relaxin. Relaxin is effective in both castrated and castrated hysterectomized guinea-pigs which have been pretreated with oestradiol, and produces relaxation in 6 hours. This is a much shorter time than that following treatment with oestradiol alone or oestradiol and progesterone. It is concluded that relaxation of the symphysis pubis of the guinea-pig may take place by means of two different procedures: (1) prolonged treatment with oestradiol which apparently has a direct affect on the symphysis and (2) treatment

with relaxin—exogenous relaxin may be injected into an oestrogen-primed guinea-pig or endogenous relaxin may be formed after treatment with oestradiol and progesterone in the presence of a uterus.

It is noted that optimum relaxation with the steroids is obtained when progesterone and oestradiol are given simultaneously. Desoxycorticosterone acetate is approximately one tenth as active as progesterone in its ability to produce the formation of relaxin and pubic relaxation.—[Author's summary.]

1809. **Relationship between Erythrocyte Sedimentation Rate, Sludged Blood, and Plasma Proteins during Pregnancy.**

By L. D. ODELL, G. T. ARAGON, and R. E. POTTINGER. *Amer. J. Obstet. Gynec.*, **54**, 596–610, Oct. 1947. 4 figs., 26 refs.

The authors apply the term "sludged blood" to blood in which microscopic agglutination occurs within venules and arterioles, with the resultant formation of intravascular cell masses. Reference is made to the work of Knisely and his co-workers who had investigated intravascular changes under normal, experimental, and pathological states. Fifty-two pregnant and non-pregnant women were selected for study. Of these 44 were pregnant and 8 were not. Of the pregnancies 21 were normal and 23 were complicated. Sixteen patients had toxaemia and 4 thrombophlebitis; 2 were suffering from acute haemorrhagic shock, and 1 had an extrauterine pregnancy. The lateral bulbar conjunctival vessels were studied by means of a Leitz dissecting microscope mounted on a colposcope stand. The size of intravascular masses and the degree of reduction of rate of flow were evaluated in fine, medium, and large venules and arterioles and from these observations an estimate was made of the erythrocyte sedimentation rate. As a check on the estimates venous blood was taken and the sedimentation rate was read in a Wintrobe tube with heparinized blood. The cell volume, fibrinogen content, total serum protein, and albumin : globin ratio were also estimated.

The result showed that the degree of "sludge" appeared to be proportional to the sedimentation rate. It was detected readily in fine venules, giving rise to the appearance of a string of beads, in the medium-sized venules with a granular appearance, and least readily in the large venules, where larger clumps were visible. "Sludge" was not observed in arterioles during normal pregnancy. The largest cell masses, and the greatest reduction in rates of flow, were seen in patients near term, in labour, or early in the puerperium. In 6 normal pregnant patients with sedimentation rates below 24 mm. per hour, no intravascular agglutination was detected. In two non-pregnant controls, with high sedimentation rates associated in one case with pelvic inflammatory disease and in the other with carcinomatosis, there was "sludging" in both venules and arterioles. In normal pregnancy all patients with a sedimentation rate of 33 mm. per hour or more were found to have "sludged blood". In pregnancy toxaemia arteriolar narrowing was detected in most patients and intravascular agglutination with reduced rate of flow was observed. "Sludge" was more pronounced than in normal pregnancy. Similarly in the cases of thrombophlebitis intravascular agglutination was marked, as it was in 3 instances of haemorrhage shock. In one case no "sludge" was detected in a patient with a low sedimentation rate, in spite of the diagnosis of acute inflammatory pelvic disease. Operation revealed the presence of an ectopic pregnancy. *J. Stallworthy*

1810. **Serum Precipitable Iodine Concentrations during Pregnancy.**

By M. HEINEMANN, C. E. JOHNSON, E. B. MAN. *J. clin. Invest.*, **27**, 91–97, Jan. 1948. 4 figs., 23 refs.

"Circulating thyroid hormone is measured more accurately by determination of serum precipitable iodine than of basal metabolic rate. Since the latter increases during pregnancy serum precipitable iodines were investigated in 43 pregnant women and followed in some subjects after delivery." Of the subjects 29 were normal. Two of these were given 15 drops daily of Lugol's solution for 5 and 9 weeks respectively. "One subject received 100,000 units of oestradiol in oil intramuscularly within 1 week. Of the remaining 14 women, 4 had hyperthyroidism, 4 miscarried, and 6 who did not miscarry were given desiccated thyroid, although the diagnosis of hypothyroidism could be made in only 1. The serum proteins were precipitated with zinc sulphate and sodium hydroxide, and the iodine included with the precipitated proteins was measured by the Riggs and Man permanganate acid ashing method. With this method the range of concentrations in normal humans is 4 to 8 μg. per cent with a mean value of 5.6 ± 1.3 μg. per cent."

In the 29 normal pregnant women the concentrations of serum-precipitable iodine ranged from 6.2 to 11.2 μg. per 100 ml., a rise in value being noted as early as 3 and 6 weeks after conception. The concentrations did not increase during the subsequent course of pregnancy, and soon returned to normal after delivery. In 10 cases women, in whom abortion threatened or had occurred, had serum-precipitable iodine values low for normal pregnancy. One patient taking gr. 3 (0.2 g.) of desiccated thyroid daily miscarried when the serum-precipitable iodine value was 7.3 μg. and aborted a second time when she was not taking thyroid and her iodine value was as low as 2.8 μg. per 100 ml. In 3 pregnant women with hyperthyroidism, concentrations of serum-precipitable iodine were higher than in normal pregnant subjects. These women

were treated with thiourea and Lugol's solution, and were delivered of apparently normal babies at term. There was 1 case of hypothyroidism, the patient taking gr. 1½ (0.1 g.) of desiccated thyroid daily in the third month. In the fourth month there was a threatened abortion and at this time the serum-precipitable iodine value was found to be 6.6 μg. per 100 ml. She was given 2 mg. of thyroxine intravenously on 2 successive days, and the oral dose of thyroid was increased. After the effect of intravenous thyroxine had subsided the serum-precipitable iodine values were 10 and 7.8 μg. per 100 ml. She was delivered of a normal baby at term. The authors consider that there may be a place for thyroid therapy in pregnancy when the serum-precipitable iodine values are low, and that such treatment may prevent abortion, although the observations they quote in this paper are statistically insignificant. *R. B. Lucas*

1811. **The Histaminolytic Action of Blood during Pregnancy.**

By G. V. Anrep, G. S. Barsoum, and A. Ibrahim. *J. Physiol.*, **106**, 379–393, Oct. 15, 1947. 4 figs., 12 refs.

The authors describe a simplified and rapid method for estimating the histaminolytic index (HI) of blood—that is, the percentage of histamine diphosphate destroyed in 30 minutes at 37° C.—the initial concentration being 3 μg. per ml. Negative findings are reported in 150 tests for histaminolysis in normal human blood, plasma, or serum. Similar results were obtained with the blood of patients with tuberculosis, cancer, allergy, and heart failure, and in various febrile states. In the blood and serum of dogs, cats, rats, and horses there was no histaminolysis, and in those of pigs, camels, sheep, and rabbits indices ranged from 15 to 30 per cent. Subcutaneous injections of histamine in dogs and human subjects did not stimulate histaminolysis. The HI was determined in 136 cases of normal pregnancy. Histaminolysis is apparent in the third month of pregnancy and increases steadily to a maximum at term. The HI rapidly declines in 48 hours after delivery to less than a quarter of the observed maximum. The low HI of foetal blood indicates that this is not the source of the high HI of the mother's blood. Extracts of placenta had a histaminolytic action 10 to 15 times greater than that of serum, and the evidence points to the placenta as the source of the histaminolytic agent. The placentae of the dog, water buffalo, cow, horse, and pig had no histaminolytic action. Histaminolysis was found in the placenta of the rat, although rat blood in pregnancy has little or no histaminolytic power. There is no marked difference between the histaminolytic power of human placental extracts obtained at early or late stages of pregnancy.

E. F. McCarthy

1812. **Function of Hyaluronidase in Fertilization.**

By C. R. Austi. *Nature, Lond.*, **162**, 63–64, July 10, 1948. 6 refs.

1813. **The Time of Conception. Is Knaus or Stieve Correct?** (Zur Frage der Empfängniszeit der Frau: Hat Knaus oder Stieve recht?)

By G. Linzenmeier. *Zbl. Gynäk.*, **69**, 1108–1110, 1947. 2 figs.

The author states that he has had a unique opportunity of studying the question whether conception can only take place during a period of a few days near the date of ovulation (Knaus) or on any day between two menstrual periods (Stieve, Caffier, and others). Many cases of rape are reported to have occurred in Karlsruhe when the town was occupied in April, 1945. The women were in a position to fix with accuracy the day, and frequently the hour, of cohabitation. Hundreds of women consulted the medical officers at the Karlsruhe Women's Hospital.

Permission having been given by the authorities to terminate pregnancies in such cases, after strict investigation and the hearing of witnesses, the author selected 67 "reliable" cases in which it was possible to ascertain with accuracy the date of cohabitation and the menstrual history of the last 6 months. He found that in no case had conception taken place during the premenstrual phase. Out of the 48 women with a history of regular 4-weekly periods, 23 had conceived during the postmenstruum and 25 during the intermenstruum. Nineteen women menstruated irregularly and of these 2 had conceived at the beginning of the premenstruum, 14 during the intermenstruum, and 3 in the postmenstruum. As controls 90 women were investigated who did not conceive as the result of forced cohabitation. In all these cases, intercourse had taken place either during the postmenstruum or during the premenstruum, never during the optimal period.

The author concludes that the probability of conception is only slightly less during the first 10 days of the cycle than between the 11th and 18th days of a 28-day cycle. Conception does not take place during the premenstruum but may occur on any other day of the cycle, with greatest facility during the well-known optimal period. Conception occurring during the postmenstruum is best explained by Caffier's theory of "provoked" ovulation. *N. Alders*

1814. **The Human Conceptus during the First Two Weeks of Gestation.**

By J. Rock and A. T. Hertig. *Amer. J. Obstet. Gynec.*, **55**, 6–17, Jan. 1948. 3 figs., 10 refs.

Early embryos were obtained from material removed at operation (26 specimens from 122 uteri removed from fertile women, 104 of whom had ovulated and had been exposed to the possibility of conception) and 4 ova were fertilized *in vitro*

by sperms. The fertilized ova could be " cultured " to the 2-cell or 3-cell stage. The earliest of the specimens obtained at operation corresponded to to a " 7-day-old " gestation. Of the operation specimens 47 per cent were abnormal [an interesting point for a discussion on the relative importance of environment versus genetic factors]. The authors consider that the ovum may reach the uterus by the third day. As judged from what is known about monkeys, a blastocyst is present by the 6th day with three differentiated tissues beginning to embed in the endometrium. By 10 days the ovum is interstitial in the endometrium and has a diameter of 0.5 mm., and the amnion is formed. By 12 days the ovum is 1 mm. in size and the embryo itself about 0.1 mm. By 14 days the mesoblast is extending and the maternal blood filling the lacunar spaces. At 16 days branched villi of a mature type have appeared.

[The work of these authors is so important and well known that this paper must be read fully.]

Kenneth Bowes

1815. **Foetal Death with Increased Length of Pregnancy.** (Fruchttod bei verlängerter Tragzeit.)

By K. SOLTH. *Geburtsh. u. Frauenheilk.*, **8**, 188–197, Jan. 1948. 4 figs., 11 refs.

An investigation was made of the foetal deaths which occurred between 1901 and 1945 in the University Clinic, Marburg. There were 15,686 births of which 585 were stillbirths. The author was particularly interested in the connexion between the duration of pregnancy and the foetal mortality. The length of gestation was estimated from the first day of the last menstrual period. A pregnancy was considered to be prolonged when it exceeded 290 days; there were 3,358 cases (22.48 per cent) in this series. The foetal mortality with varying lengths of pregnancy was: 18.88 per cent for 220 to 239 days; 8.85 per cent for 240 to 259; 3.09 per cent for 266 to 279; 2.68 per cent for 280 to 299; 6.13 per cent for 300 to 319; and 9.92 per cent for 320 to 339 days. These figures show that the mortality rate is high among the premature infants and also in those postmature after the 290th day. The author investigated the weight and length of the postmature babies, and found that 70 per cent were of normal weight and size. The highest death rate was in the remaining 30 per cent—that is, in infants larger or smaller than normal. When the foetus weighed between 4,500 and 5,000 g. the foetal mortality was 6.12 per cent; when the weight was between 5,500 and 6,000 g. it was 50 per cent. When the foetus weighed less than 2,000 g. the mortality was 60 per cent; when less than 2,500 g. it was 20 per cent. The author concluded that the high foetal mortality in prolonged pregnancy was due to the relatively high proportion of overdeveloped and underdeveloped foetuses.

Gladys Dodds

1816. **Postmaturity.**

By L. A. CALKINS. *Amer. J. Obstet. Gynec.*, **56**, 167–172, July 1948. 2 figs.

1817. **Hormone Secretion by Human Placenta Grown in Tissue Culture.**

By H. L. STEWART, M. E. SANO, and T. L. MONTGOMERY. *J. clin. Endocrinol.*, **8**, 175–188, Feb. 1948. 8 figs., 11 refs.

Since the observations that the blood and urine of pregnant women contain large amounts of gonadotrophins and oestrogens, and that placental extracts also contain these hormones, the placenta has been regarded as an organ of internal secretion. Recent work on tissue culture has supported this view, and this paper is a further contribution to the evidence that the placenta is the organ responsible for secreting the hormones of pregnancy. Placental fragments for tissue culture were obtained during operations for termination of pregnancy. The tissue was examined histologically and cultured, and the hormones secreted in culture were assayed biologically. The preoperative levels of serum gonadotrophin and oestrogen were also recorded in each case. From this work [4 cases are described in detail, but it is clear that many others were studied] the authors draw the following conclusions: (1) Three types of cell can be grown from placental tissue—stromal, syncytial, and Langhans cells—but after a few days the Langhans cells predominate, the syncytial cells growing very slightly and eventually disappearing altogether. (2) Gonadotrophic hormone is produced by tissue cultures of 3-month-old human placentae. (3) The amount of gonadotrophin secreted is directly related to the growth of Langhans cells. (4) Evidence of oestrogen production is inconclusive; the blood level of oestrogen is highest just before delivery, but it was found impossible to grow tissue cultures from placentae of 8 and 9 months, as the fibrous stroma grew rapidly and inhibited the growth of the other cell types, which presumably are responsible for hormone production. (5) Control tissue cultures of fibroblasts do not secrete hormones.

[A detailed description is given of the methods of tissue culture and hormone assay employed, and the article is accompanied by a series of excellent photomicrographs.] *Margaret Puxon*

1818. **Enhancement of Effect of Chorionic Gonadotrophin on Ovarian Hyperemia in the Rat by Pituitary Extract.**

By A. E. RAKOFF and P. H. FRIED. *Proc. Soc. exp. Biol., N.Y.*, **66**, 491–492, Nov. 1947. 16 refs.

Intraperitoneal injections of chorionic gonadotrophins, pituitary " synergist ", or a mixture of both were given to 307 albino rats, 28 to 32 days old. The unit of " synergist ", prepared from sheep pituitary, was defined as that amount which, when combined with 15 i.u. chorionic gonadotrophin,

will cause a five-fold increase in ovarian weight over that of uninjected controls. The rats after 1 hour and 1½ and 2 hours were asphyxiated with ether and the ovaries were examined for hyperaemia. Technical details are given by Kupperman and Greenblatt (*Sth. med. J.*, 1946, **39**, 158). The authors maintain that the addition of small amounts (0.044 unit) of "synergist" enhances the value of the rat test for pregnancy. *Magnus Haines*

1819. **The Guterman Reaction in Clinical Practice.**
By E. M. A. Day and L. J. Cains. *Med. J. Aust.*, **1**, 199–201, Feb. 14, 1948. 4 refs.

The authors have investigated a series of cases to determine whether the Guterman test for urinary pregnanediol is reliable enough for use as an aid in the diagnosis of pregnancy. All reagents were carefully purified, as previous results had shown that impurities, especially in the sulphuric acid, were a potent source of error.

One series of 18 specimens of urine submitted for the Friedman test were also examined for the Guterman reaction. With the Friedman test there were 9 positive reactions, 8 negative reactions, and 1 doubtful reaction. With the Guterman test there were 15 positive and 3 negative reactions. In all these cases subsequent events proved the Friedman reaction to be the correct one. Of 13 normal pregnant women attending the antenatal clinic, only 10 gave a positive Guterman reaction. In a variety of other conditions, including foetal death and hydatidiform mole, the rate of error with this test was high. In all, "the total error in the series was 36 to 27 per cent 'false positive' reactions and 9 per cent 'false negative' reactions". As 8 positive results were given by urine from men, it is suggested that the test may be non-specific.
Doreen Daley

1820. **A Chemical Test for Pregnancy: Estimation of Pregnanediol Glycuronate.** (Un test chimique de la grossesse: Le dosage du glycuronate de prégnandiol.)
By R. Rivoire and G. Bueil. *Sem. Hôp. Paris*, **24**, 1634–1636, July 2, 1948. 8 refs.

1821. **The Male Frog, *Rana pipiens*, as a New Test Animal for Early Pregnancy.**
By P. B. Wiltberger and D. F. Miller. *Science*, **107**, 198, Feb. 20, 1948. 2 refs.

This test for pregnancy is carried out by injecting 5 ml. of morning urine into the lymph-sac of each of two male frogs, which are then placed in individual clean jars. A positive response is indicated by the presence of sperm in the urine, which 4 hours after the injection is examined microscopically in two portions, that voided in the interval and the portion in the bladder (and voided on disturbance of the frog). No false results were given in 200 tests on urine from men, non-pregnant women, and women during the first three months of pregnancy. False-negative results may be obtained in tests of urine from women later in pregnancy. The frogs may be used again after 4 to 5 days. *Peter C. Williams*

1822. **Protein—its Importance in Nutrition of Pregnancy.**
By C. H. Boso. *West Virginia med. J.*, **44**, 213–217, Aug. 1948. 20 refs.

1823. **Eclampsia.**
By R. E. Jones. *J. med. Ass., Georgia*, **37**, 207–212, June 1948.

1824. **Eclamptic Toxaemia.**
By D. N. Henderson. *Bull. Vancouver med. Ass.*, **24**, 261–267, May 1948.

1825. **Influence on the Infant of Toxaemias of Pregnancy.** (Uber den Einfluss der Graviditätstoxikose beim Kind.)
By W. Neuweiler. *Gynaecologia, Basel*, **125**, 24–29, Jan.–Feb. 1948. 5 figs.

The author reviews the effects of toxaemia of pregnancy on the foetus in 400 cases seen at the

Table I.
Duration of Pregnancy and Stillbirths, Neonatal Deaths

Duration of Pregnancy	"Toxic" Cases		"Normal" Mothers	
	Still-births	Neonatal Deaths	Still-births	Neonatal Deaths
	(%)	(%)	(%)	(%)
40 weeks	5.4	4.8	0.6	0.5
32 to 36 weeks	25.0	10.5	7.6	9.2
28 to 32 weeks	Total 88.7%			

Table II.
Grade of Toxaemia and Stillbirths, Neonatal Deaths

Grade of Toxaemia	Stillbirths	Neonatal Deaths
	(%)	(%)
Albuminuria	2.22	2.22
Pre-eclamptic toxaemia	1.96	11.76
Eclampsia	10.64	7.45

Table III.
Method of Delivery

Method of Delivery	"Normal" Mothers	"Toxic" Cases
	(%)	(%)
Normal	91	65
Extraction	4	1.5
Caesarean section	2.5	28
Forceps	2	5
Perforation	0.5	0.5

University Clinic, Berne, over a period of 25 years. He classifies toxaemia into: albuminuria of pregnancy, severe pre-eclamptic toxaemia, and eclampsia. All the findings can be given in the simplified tables above.

"Toxaemia" developed in 0.4 per cent of all pregnant women between 1917 and 1924 and in 1.3 per cent between 1925 and 1940. The figure now stands at about 0.9 per cent. The children of "toxic" mothers tend to be not only lighter but also shorter at birth. *Elliot E. Philipp*

1826. **A Nine-year Follow-up in Cases of Toxemia of Pregnancy.**

By F. P. LIGHT. *Amer. J. Obstet. Gynec.*, **55**, 321–325, Feb. 1948. 3 figs., 10 refs.

Since 1937 patients treated for toxaemia of pregnancy at the Long Island College Hospital have attended a follow-up clinic. Of 530 toxaemic patients 391 were followed up; there were 968 pregnancies among these 391 patients, 685 of which were associated with toxaemia or vascular renal disease; the remaining 283 were normal. Only 13 of the patients had eclampsia. The duration of the toxaemia and the influence of toxaemia on permanent renal damage were studied.

The patients were divided into five groups—those who had severe toxaemia for 1 week, 2, 3, 4, or over 4 weeks respectively. There was no significan difference between the groups. In some 30 per cent there was permanent damage; for the most part the evidence for this was an elevated blood pressure. The cases were also grouped according to the patient's age at the time of the onset of toxaemia. The table shows a definite relation between the age of the patient at the time of the toxaemia and the incidence of the residual damage.

Late damage increased progressively with age.

Age	18 to 20	21 to 25	26 to 30	31 to 35	Over 35
Total cases	61	118	91	47	61
Residual damage	9	25	26	23	32
Percentage of residual damage	13.1	21.2	28.5	48.9	52.4

It would seem, therefore, that age rather than the duration of the toxaemia is the determining factor in permanent renal damage, and it may well be that at least some of these patients would have suffered from hypertension at this particular time of life had all their previous pregnancies been normal or even had they never been pregnant.

D. M. Stern

1827. **Anuria in Eclampsia Effectively Treated by Intravenous Procaine.** (Anúria en la eclampsia: su tratamiento eficaz por la novocaina intravenosa.)

By M. B. R. LÓPEZ. *Obstet. Ginec. lat.-amer.*, **6**, 44–51, Jan.–Feb. 1948.

Eclampsia is only a single manifestation of the eclamptic syndrome, which may be associated with other features such as haemorrhage. Aetiologically, modern opinion tends to incriminate the placenta, "that endocrine gland suddenly implanted into the hormonal system". A disturbance of endocrine balance leads in its most advanced stage to the convulsions of eclampsia. Anuria may be a feature of convulsive toxaemia. Deficient blood supply in the affected organs leads to haemorrhage, degeneration, and necrobiosis. It is suggested that the intravenous injection of procaine may act in these cases of anuria as in other cases associated with spasm, such as bronchial asthma and spasmodic conditions affecting the retinal vessels. Procaine is given intravenously, 10 ml. of a 1 per cent solution being administered in 5 minutes. A careful watch is kept on the pulse rate, blood pressure, and general condition. The same dose is repeated in 6 hours. Two cases are described in which this treatment was successful in inducing diuresis. In both, anuria followed eclampsia, lasting for 36 hours in one case and 30 hours in the other. In both cases the blood pressure fell and diuresis was rapidly established. The authors conclude that this is a valuable method of treatment, and that it should be instituted early to prevent permanent total renal failure.

[In both these cases hypertonic glucose was given with the procaine, one patient receiving insulin as well. It appears, therefore, that the evidence for the effect of procaine is inconclusive. Cases of total anuria after eclampsia or accidental haemorrhage constitute a difficult clinical problem. In some of these, the condition proves to be a cortical necrosis of the kidneys and death from uraemia ultimately results. Where recovering occurs, the nature of the renal lesion is less certain. The method described here might well be tried in cases of anuria with severe toxaemia but, until a large series of cases has been studied, no definite conclusion can be reached. It is possible that the patients described here might have recovered without treatment, or that the hypertonic glucose may have been responsible for the diuresis.]

Josephine Barnes

1828. **A Clinical Study of Toxemias of Pregnancy. Analysis of a Ten Year Period.** [In English.]

By I. LIQUORNIK and E. RABAU. *Gynaecologia, Basel*, **126**, 7–21, July 1948. 18 refs.

1829. **Prophylaxis as well as Therapeusis in Toxemia of Pregnancy.**

By G. G. GREENE. *Kentucky med. J.*, **46**, 100–104, Mar. 1948. 6 refs.

1830. **Histidine and Histamine Metabolism in Normal and Toxaemic Pregnancy.** (Ueber den Histidin- und Histaminstoffwechsel in der normalen und toxämischen Schwangerschaft.)

By R. KAPELLER-ADLER, *Wein. klin. Wschr.*, **60**, 395–398, June 25, 1948. 46 refs.

1831. **The Expectant Management of Placenta Previa.**

By T. J. WILLIAMS. *Amer. J. Obstet. Gynec.*, **55**, 169–176, Jan. 1948. 7 refs.

The results of treatment of 105 cases of placenta praevia at the University of Virginia Hospital during the past 11 years are reviewed. In 41 patients treatment was expectant. The method of treatment and delivery is set out in the following table.

Method of Treatment and Delivery

Method	No.	Per cent
Caesarean section	44	42
Rupture of membranes	32	30
Scalp traction after rupture of membranes	2	2
Spontaneous onset of labour and delivery	20	19
Version	7	7
Total ...	105	100

Treatment was active if labour had begun or if the patient was at or near term. In 22 cases classical Caesarean section and in 22 the lower-segment operation were performed. All patients with central placenta praevia were delivered by Caesarean section. It is interesting to note that in 64 patients an attempt was made to diagnose the site of the placenta by various methods of X-ray examination. In 51 of these the X-ray diagnosis was helpful, and in 13 the findings were not conclusive.

There was one maternal death in the series, due to generalized infection on the 5th postpartum day. Twenty-nine children died; 14 were stillborn, and 15 died neonatally. Of these, 10 per cent were in cases treated at or near term and 68 per cent in cases in which pregnancy was terminated before the child attained a weight of 2,500 g.

The treatment of placenta praevia is discussed in detail and follows the usual lines. In some instances, where the presenting part is high and it has been decided to deliver the patient, vaginal examination is not made and the patient is delivered by Caesarean section. By this means some cases of bleeding from a placenta in a normal situation will be treated by Caesarean section, but the author does not consider this a disadvantage. Patients with antepartum haemorrhage should be admitted to hospital. Some [type of patient not specified] are allowed home " with instructions to abstain from sexual intercourse, to permit no vaginal examinations, and to return to the hospital with the first recurrence of bleeding ". In 41 cases in which management was expectant there were 5 foetal deaths and 4 premature deliveries; 1 baby born at term died of congenital defects.

[This paper and the discussion which follows should be read together with the following: (1) Macafee, *J. Obstet. Gynaec. Brit. Emp.*, 1945, **52**, 313; (2) Sturrock *et al.*, *Edinb. med. J.*, 1947, **54**, 496.] *G. Gordon Lennon*

1832. **Retroperitoneal Haemorrhage in Pregnancy.**

By J. K. OGDEN. *Brit. med. J.*, **1**, 389–391, Feb. 28, 1948. 6 refs.

The author describes a case of eclampsia with concealed accidental haemorrhage complicated by a fatal retroperitoneal haemorrhage in the post-operative puerperal stage. The eclampsia occurred at 35 weeks and was accompanied by concealed accidental haemorrhage and marked shock. Conservative treatment was adopted and the patient responded well. A further retroplacental haemorrhage necessitated surgical intervention and a classical Caesarean section was performed; the foetus was macerated. Convalescence was proceeding normally when early on the 4th day the patient suddenly collapsed with signs of internal haemorrhage, failed to respond to resuscitation, and died in 2 hours. Necropsy revealed changes in the liver, kidneys, and spleen consistent with the degree of toxaemia and repeated haemorrhages, and also a severe retroperitoneal haemorrhage, involving mainly the area within the curve of the duodenum but causing rupture of the floor of the lesser sac and massive intraperitoneal haemorrhage. The actual site of the bleeding was not found.

The literature is reviewed; of the 6 reported cases it is observed that in 5 the haemorrhage started in the region of the lesser sac and these were all fatal; in the 1 case in which it started in the pelvic area the patient recovered. It is also noted that in 2 of the previously reported cases toxaemia existed, and it is suggested that this may be of aetiological significance in view of the capillary thrombosis with extravasation of blood which is known to occur in eclampsia. *Hugh R. Arthur*

1833. **Management of Late Hemorrhages of Pregnancy.**

By J. H. BLOOMFIELD. *Wisconsin med. J.*, **47**, 287–290, Mar. 1948.

1834. **The Influence of the War Period on Pregnancy. IV. Influence on Abortions and Premature Deliveries.** (Indagini cliniche e considerazioni circa l'influenza del periodo bellico sullo stato puerperale. IV. Influenza sugli aborti e sui parti prematuri.)

By S. CANNA. *Ginecologia, Torino*, **13**, 515–531, Nov. 1947. 8 figs., 49 refs.

The incidence of abortion and premature delivery was studied at the Obstetric School of Novara between 1933 and 1945. Before the war the incidence of abortion in 4,523 pregnant women was 12.2 per cent; during the war it was 15.4 per cent in 4,113 cases. The figures for primiparae were 6.7 and 9 per cent; for multiparae they were 16.5 and

20.6 per cent respectively. For women living in towns the incidence was 10.8 per cent in peacetime and 12.8 per cent in wartime; for those living in the country the figures were 13.7 and 17.6 per cent. The incidence in housewives was 11.7 per cent in peace time and 14.5 in wartime; in factory workers 12.1 and 14.2 per cent; in land workers 14.4 and 21.4 per cent. During the war there was a general slight increase in the incidence of abortion in both primiparae and multiparae. The increase was more pronounced in land workers. The incidence of premature delivery was 13.8 per cent in peacetime and 21.4 in wartime. This increase was more accentuated in women living in towns and in factory workers.

The author does not consider that abnormal condition of the genital organs or of the ovum, or dysfunction of the endocrine gland, caused the increase in abortion and premature delivery. The incidence of acute infectious diseases did not increase during the war; but there was an increase in the incidence of syphilis during the war. According to Roberto, emotional shock is not a cause of abortion or premature delivery; during the earthquake at Lacedonia in 1930 no abortions occurred among 191 pregnant women. The author believes that the deficiency of fat-soluble vitamins in the diet during the war was a cause of increased interruption of pregnancy. *Rina Saunders*

1835. **Technique of Therapeutic Abortion.** (A propos de la technique de l'avortement thérapeutique.)

By L. PORTES, M. MAYER, A. GRANJON, and M. BOMMELAER. *Gynéc. et Obstét.*, **47**, 185–192, 1948. 13 figs.

There still remain certain cases where therapeutic abortion is legally justifiable. According to Balard, Broustet, and Mahon, the technical problem depends on the rapidity and simplicity of the operation, the duration of pregnancy, the condition of the cervix, the possible need for sterilization, and the mode of anaesthesia. They recommend curettage in the first 2 months and abdominal Caesarean section under local analgesia from the third till the 7th month.

The present authors consider that dilatation of the cervix may be dangerous, especially when tents are used, and that local analgesia may be quite inadequate. They distinguish two types of case: (1) Conservative therapeutic abortion is indicated when there is a threat of an accident which may endanger the patient's life, although the possibility of future pregnancies has to be considered. Physiological saline is injected into the amniotic cavity after transabdominal puncture with a spinal-puncture needle. Pressure is measured with the Claude manometer. After amniotic fluid has been allowed to flow out [the authors do not state to what extent] the saline solution is injected until the pressure is double the initial pressure. Two to 3 such "lavages" are performed, the amount of saline (and consequently the intrauterine pressure) being augmented each time. The authors have used opaque solutions and carried out the manipulations under radioscopic control. The needle is withdrawn after a final injection. Usually, labour sets in within 24 hours. If pains have not started 8 hours after the 1st injection, a 2nd injection on the 3rd day is followed by the onset of labour. Expulsion is complete.

(2) In cases where the mother's condition precludes further pregnancy, therapeutic abortion is carried out by vaginal hysterotomy with ligation of the tubes. Vaginal hysterotomy, though less traumatizing than abdominal hysterectomy, is only performed in multiparous women who have been pregnant less than 3 months; this ensures that exteriorization of the uterus and tubal ligation and section can be carried out. On the evening before operation the vagina is packed with gauze dipped in a solution containing 100,000 units of penicillin. The authors usually operate under epidural or spinal analgesia. The operation consists, briefly, in an anterior longitudinal colpotomy, vaginal exteriorization of the fundus (if necessary, at 2½ to 3 months after puncture of the amnion), median hysterotomy on the posterior surface of the uterus, enucleation of the ovum (often spontaneous), suture of the uterine incision with two continuous sutures, exteriorization, double ligature, and section between the two ligatures of both tubes with subsequent burying of the medial stumps under the anterior uterine peritoneum, reposition of the uterus, and suture of the colpotomy incision in the usual manner. The patient receives 200,000 units of penicillin per day during the 5 following days. *H. Godar*

1836. **Immediate Foetal Death After the Use of the Root of Saponaria in Artificial Abortion.** (Müvi vetélés kapcsán szappangyökérrel közvetlenül okozott magzati halál.)

By J. GAÁL. *Orv. Lapja*, **4**, 14, Jan. 4, 1948. 2 figs.

Artificial abortion is still prevalent in Hungary despite vigorous measures against it. Mechanical methods are most commonly used, and among them the introduction of the sharpened root of saponaria into the uterus is particularly popular. In the case reported here a pregnancy of 4 months' duration was terminated in this way. The root had perforated the abdominal wall of the foetus, damaged its abdominal organs, pierced the diaphragm, and injured the heart. Apparently the wall of the uterus was damaged as well, but the injury was not perforating. After instrumental evacuation of the uterus and treatment with penicillin and sulphathiazole the woman, who had been admitted to hospital with fever and rigors, rapidly recovered. *Vilma Samet*

1837. **A Clinical and Histopathologic Study of Lesions of the Cervix Uteri during Pregnancy.**

By C. F. FLUHMANN. *Amer. J. Obstet. Gynec.*, **55**, 133–150, Jan. 1948. 13 figs., 9 refs.

The basis of this study is an analysis of the findings in a series of 89 cases of gross abnormality of the cervix in which a biopsy was obtained or hysterectomy was performed. All stages of gestation are represented. The lesions encountered were: cervical polypi, 37; so-called erosions, 32; carcinoma, 10; condyloma acuminata, 5; endometrial polypi, 3, leucoplakia, 2. The author reviews the literature on the normal cervix in pregnancy.

To obtain information on erosion of the cervix during pregnancy a series of 119 consecutive cases (all private patients) was analyzed. The results are given in the following table.

Incidence of so-called Cervical Erosion at First Prenatal Visit.

Month of Pregnancy	Gravida I		Gravida II or More		Total	
	Erosion	No Erosion	Erosion	No Erosion	Erosion	No Erosion
2	11	22	6	12	17	34
3	10	6	5	5	15	11
4	3	0	1	7	4	7
5	6	2	3	0	9	2
6	2	1	1	3	3	4
7	2	0	3	0	5	0
8	3	3	1	0	4	3
9	0	0	0	1	0	1
Total	37	34	20	28	57	62

At the first antenatal examination an erosion was seen in 48 per cent of all groups. There was little difference between primigravidae and multigravidae.

There were no associated symptoms in 19 out of the 32 so-called erosions. There was spontaneous bleeding in 6 cases, and "spotting" or blood-tinged discharge in 5. The histological changes at the sites of the erosions varied greatly and are considered under the following headings: (*a*) adenomatous proliferation of the glands; (*b*) papillary outgrowths; (*c*) oedema and increased vascularity; (*d*) infiltration with inflammatory cells; (*e*) epidermization, with hyperactive basal cells and hypertrophy of squamous epithelium; (*f*) formation of decidua. The author considers that although some cervical erosions result from an inflammatory condition which may have existed before pregnancy, most of the cervical erosions seen during pregnancy are not the result of cervicitis but represent a type of adenoma. *C. Gordon Lennon*

1838. **Conception, Pregnancy, and Labour in a Case of Submucous Fibroids.** (Konzeption, Gravität und Partus bei submukosen Myom.)

By H.-W. KAYSER. *Zbl. Gynäk.*, **69**, 1244–1248, 1947. 2 figs., 42 refs.

1839. **Uterine Fibroids in Pregnancy and the Puerperium.** (Fibromiomi uterini in gravidanza ed in puerperio.)

By G. TARICCO. *Ginecologia, Torino*, **14**, 257–272, June, 1948. 1 fig., bibliography.

1840. **Torsion of a Pregnant Uterus with Rupture.**

By S. L. SIEGLER and L. M. SILVERSTEIN. *Amer. J. Obstet. Gynec.*, **55**, 1053–1057, June, 1948. 1 fig., 16 refs.

1841. **Hydatidiform Mole in a Twin Pregnancy with a Viable Foetus.**

By H. V. MISHLER, G. R. DICKERHOOF. *Ohio St. med. J.*, **44**, 714–715, July, 1948. 13 refs.

1842. **Massive Gastric Hemorrhage in Pregnancy.**

By J. CARANGELO and T. D. EFSTATION. *Amer. J. Obstet. Gynec.*, **56**, 191–194, July, 1948. 4 refs.

1843. **Pregnancy Following an Interilio-abdominal Amputation. (Sacroiliac Disarticulation or Hemipelvectomy.)**

By H. L. WILCOX. *Amer. J. Obstet. Gynec.*, **55**, 1068–1070, June 1948. 2 figs., 2 refs.

1844. **Intestinal Obstruction in Pregnancy Due to Volvulus of Sigmoid.** (Obstrucão intestinal na gravidez por volvo do sigmoide.)

By J. AMORIM, A. R. MARTÍNEZ, and L. DE ALMEIDA. *Obstet. Ginec. lat.-amer.*, **6**, 165–173, May 31, 1948. 3 figs., 31 refs.

1845. **Peptic Ulcer during Pregnancy with a Report of a Case of Perforation.**

By D. W. JAMES. *Brit. med. J.*, **2**, 74–75, July 10, 1948. 6 refs.

1846. **Acute Leukaemia and Pregnancy.** (Leucemia aguda y embarazo.)

By J. BAZÁN, F. A. U. IMAZ, and J. A. FERNÁNDEZ. *Obstet. Ginec. lat.-amer.*, **6**, 145–164, May 31, 1948. 6 figs., 31 refs.

1847. **Pregnancy Associated with Polyostotic Fibrous Dysplasia.**

By R. B. NELSON. *Med. Ann. Distr. Columbia*, **17**, 157–159 and 189–190, Mar. 1948. 4 figs., 4 refs.

1848. **The Influence of the War Period on Pregnancy. III. Influence on Sympathetic Disturbances.** (Indagini cliniche e considerazioni circa l'influenza del periodo bellico sullo stato puerperale. III. Influenza sui fenomeni simpatici.)

By S. CANNA. *Ginecologia, Torino*, **13**, 497–514, Nov. 1947. 4 figs., bibliography.

The author has continued his series of investigations into the influence of war conditions on pregnancy. He presents a comparative and statistical survey of disturbances of the sympathetic nervous system during peace and war and in 8,636 cases at the Obstetric School of Novara between 1933 and 1945. The patients were divided into:

(1) housewives; (2) factory workers and land workers. Primiparae and multiparae were investigated separately. A further two groups consisted of women living in town and country. The influence of war conditions on pregnant women was undoubtedly related to their social condition and to their parity. The number of cases without sympathetic disturbances increased progressively between 1933 and 1945, with a minimum of 16.2 per cent in 1934 and a maximum of 40.5 per cent in 1945, and the number in which sympathetic disturbances were very accentuated decreased progressively during the same period, with a maximum of 30 per cent in 1935 and a minimum of 5.1 per cent in 1945. For primiparae without sympathetic disturbances the figures were 29.7 per cent before the war and 35.4 per cent in wartime; for multiparae they were 23.7 and 36.2 per cent. The decrease in incidence of pronounced sympathetic disturbances was greater in multiparae. There were no great differences in this respect between urban and rural dwellers. The decrease in incidence of accentuated sympathetic disturbances was most evident in housewives (from 25.7 per cent before the war to 7.1 per cent during the war).

Many authors have suggested that the cause of sympathetic disturbances in pregnancy is hyperexcitability of the nervous system. If this were the case the war should have brought about an increase in such phenomena. Endocrine and ovarian factors are also unrelated to the observed fall in incidence of sympathetic disturbances. It is thought that diet played an important part.

Rina Saunders

1849. **The Determination of the Prognosis of Pregnancy in Rheumatic Heart Disease.**

By J. J. BUNIM and J. RUBRICIUS. *Amer. Heart J.*, **35**, 282–297, Feb. 1948. 1 fig., 58 refs.

Observations were made in 142 pregnant women with rheumatic heart disease through pregnancy and the puerperium; the literature on the subject was studied. It is concluded that pregnancy itself has little effect on the prognosis in rheumatic heart disease.

H. E. Holling

1850. **Maternal Rubella During Pregnancy as Cause of Congenital Cataract and Other Congenital Malformations.** [In English.]

By M. BARDRAM and P. BRÆNDSTRUP. *Acta ophthal., Kbh.*, **25**, 353–367, 1947. 32 refs.

This paper reviews the evidence that an attack of rubella in the first 3 months of pregnancy may cause cataract and other malformations in the baby. The histories of 8 Danish cases of malformations in the child after maternal rubella are reported in detail. In these children, one of whom was stillborn and one of whom died at 6 months, the following malformations were seen: cataract (7 cases), microphthalmus (1 case), pigmentary degeneration of retina (3), incomplete iris coloboma (1), morbus cordis (5), peculiarly long trunk (1) long fingers and toes (1).

A. Pirie

1851. **Some Virus Diseases During Pregnancy and Their Effect on the Foetus.** (Nagra virussjukdomar under graviditet och deras verkan på fostret.)

By H. GRONVALL and P. SELANDER. *Nord. Med.*, **37**, 409–415, Feb. 27, 1948. 43 refs.

In 1941 Gregg of Sydney observed congenital cataract and other abnormalities of the eyes as well as heart disease in 13 children whose mothers had suffered from rubella early in pregnancy. Adding 65 similar cases observed by his colleagues, Gregg found among the total of 78 mothers as many as 68 with a history of rubella.

The present authors have extended the study of this phenomenon to various other virus diseases in Sweden and to the question whether rubella has the same teratogenous action in Sweden as it seems to have in Australia. Their investigation was started in September 1945, in hospitals in Stockholm, Lund, Malmö, Uppsala, Gothenburg, and Kristianstad. The investigation followed two lines: (1) an examination of children whose mothers had suffered from such diseases as rubella, measles, chickenpox, mumps, infective hepatitis, or anterior poliomyelitis during pregnancy; (2) a search for records of virus diseases during the pregnancies of the mothers of children suffering from certain deformities. Scarlatina, though not a virus disease, was included in this investigation as it has been thought to damage the foetus.

The findings of this investigation are incorporated in 5 tables, which deserve study in the original. Table 4, on the frequency of certain virus diseases during the pregnancies of mothers giving birth to congenitally defective infants, shows that among 354 such mothers there were 5 who had rubella, 1 measles, 1 chickenpox, and 5 mumps during pregnancy. There were also at least 3 who had suffered from hepatitis, and at least 2 from poliomyelitis. Thus 5.1 per cent of these mothers had suffered from some virus disease during pregnancy. According to Table 2, there had been a virus disease in only 0.47 per cent of the many thousands of mothers who were confined in maternity hospitals and who served as controls. This suggests that the virus diseases in question were about 10 times as frequent among the mothers of defective infants as among the controls.

The authors conclude that rubella, mumps, infective hepatitis, and anterior poliomyelitis may injure the foetus, though rubella in this respect may be much less dangerous in Sweden than it seems to be in Australia; in the latter country it has been suggested that rubella early in pregnancy is an indication for inducing abortion. More light would be thrown on this problem if notification of these virus diseases as soon as they occur in pregnancy were made compulsory.

Claude Lillingston

1852. **Diaphragmatic Herniae as a Problem for the Obstetrician.** (Uber die zwerchfellbruche als problem des obstetrikers.)

By O. KINNUNEN. *Ann. chir. gyn. fenn.*, **37**, 193–206, 1948. 2 figs., 15 refs.

1853. **Effect of Pregnancy on the Course of Experimental Hypertension.**

By A. GROLLMAN. *Amer. J. Physiol.*, **151**, 373–379, Dec. 1947. 25 refs.

At the Southwestern Medical College in Dallas, Texas, hypertension was induced in rats, rabbits, and dogs by applying a constricting figure-of-eight band either to both kidneys, or to one kidney, the other being removed. This induced a chorionic constant elevation of blood pressure without a malignant phase. Blood pressure in the rat was determined by plethysmograph, in the rabbit by auscultation over the abdominal aorta, and in the dog by a direct mercury manometer reading after femoral-artery puncture. In hypertensive rats (36 animals) pregnancy caused a fall in blood pressure varying between 10 and 65 mm. Hg, except in 1 case. Pseudo-pregnancy induced by stimulating the cervix also induced a fall in blood pressure. The larger the litter the greater the fall. Rabbits ovulate only with coitus. In 20 pregnant animals changes were similar to those found in the rat, and again the larger the litter the greater the fall in blood pressure. Five pregnancies were observed in 3 bitches; there was only a moderate fall in blood pressure during the second half of pregnancy. The larger the animal the smaller is the size of the products of conception relative to the maternal mass; the larger the animal also the smaller is the fall in blood pressure in the hypertensive pregnant female. These findings support the contention that essential hypertension itself is not an indication for terminating pregnancy. Eclampsia is an acute condition due to the elaboration by the ischaemic kidney of a pressor agent, not elaborated in chronic hypertension. *Elliot E. Philipp*

1854. **The Rh Negative Mother in Private Obstetrical Practice.**

By R. A. WEST and N. C. SIEBERT. *J. Kansas med. Soc.*, **49**, 285–286, July 1948. 9 refs.

1855. **Pregnancy and Tuberculosis.** (Zwangerschap en longtuberculose.)

By G. LAM. *Geneesk. Gids.*, **26**, 335–339, July 15, 1948.

1856. **The Pathergic State in Various Phases of Pregnancy and the Puerperium in Tuberculous Women.** (Lo stato patergico nelle varie fasi di gravidanza ed in puerperio, in donne affette da esiti di forme tubercolari.)

By A. BORSO. *Ginecologia, Torino*, **14**, 189–201, May 1948. 4 figs., 20 refs.

1857. **Ectopic Pregnancy.**

By W. D. BEACHAM, C. G. COLLINS, E. P. THOMAS, and D. W. BEACHAM. *J. Amer. med. Ass.*, **136**, 365–371, Feb. 7, 1948. 8 figs., 14 refs.

The authors reviewed the series of 1,059 patients with ectopic pregnancy admitted to the New Orleans Charity Hospital since 1906. The incidence varied from 2.79 per cent of the obstetrical admissions in the case of white women and 1.96 per cent in the case of negresses, to 0.95 per cent and 0.59 per cent respectively during the four 10-year periods. It is believed that the lower figure of 0.59 per cent more accurately represented the correct incidence in relation to gestation at term. When these figures were compared with the gynaecological admissions it was found that the incidence was higher in the negro race than in the white. Salpingitis was also more common in negresses. Most cases in the negro group occurred in patients between the ages of 21 and 30, while in the white group the greatest incidence was between the ages of 26 and 35. In 97 per cent of the cases the chief complaints were pain, pain and bleeding, or bleeding. Amenorrhoea for 2 months before the onset of other symptoms occurred in 18.5 per cent of the cases, while 14.3 per cent had 3 months' amenorrhoea. In 1.71 per cent the symptoms developed during an apparently normal period, while 4.7 per cent stated that they had had a a normal period a fortnight before.

The authors explain the importance of a gentle but careful pelvic examination in all suspected cases, and advise exploratory puncture of the pouch of Douglas where there is doubt. The leucocyte count was found to be of little value in differential diagnosis. A correct preoperative diagnosis was made in 82 per cent of cases in the last decade. The treatment varied from unilateral salpingectomy to hysterectomy, which was performed 63 times in the last 373 cases with 11 deaths in this series. *J. Stallworthy*

1858. **On Hysterosalpingography and Extra-uterine Pregnancy.** [In English.]

By H. SKJOLBORG. *Acta radiol., Stockh.*, **29**, 456–460, May 31, 1948. 4 figs., 12 refs.

1859. **Further Observations on Ectopic Pregnancy.**

By F. E. WHITACRE and T. BRYAN. *J. med. Ass. Alabama*, **18**, 1–4, July 1948.

1860. **Congenital Absence of One Ovary Associated With Contralateral Tubal Pregnancy.**

By J. A. KURCZ and M. S. SHARP. *Amer. J. Obstet. Gynec.*, **55**, 1065–1067, June 1948. 9 refs.

1861. **The Diagnosis and Treatment of Abdominal Pregnancy.**

By F. E. WHITACRE and H. D. LYNN. *Sth. Surg.*, **13**, 635–644, Sept. 1947. 2 fig., 15 refs.

A series of 12 abdominal pregnancies is reported. Secondary abdominal pregnancy is far more

common than primary abdominal pregnancy. The existence of the latter is often doubted; the condition is more likely to be secondary to tubal abortion or rupture.

Cases in which there is no evidence of origin from a primary intrauterine or intratubal position and in which the ovary is not involved in the placental site are designated cases of primary abdominal pregnancy. The number of such proved cases is small. There are two types of secondary abdominal pregnancy—the intra-peritoneal and the intra-alimentary. The authors' 12 cases occurred among 13,926 deliveries. There were no maternal deaths, although maternal and foetal mortality was high in other series quoted from the literature. Correct diagnosis before operation is not easy. The history of the case and a careful examination of the patient should suggest the presence of abdominal gestation. Hysterography has been used in diagnosis, as also have pneumoperitoneograms and amniography.

The ages of the patients ranged from 19 to 39 years, the average being 29.4 years. Three of the patients had had no children. In 4 of the patients pregnancy had continued for 4 months, in 3 for 5 months, in 1 for 7, and in 1 for 8 months; there were 3 full-time pregnancies. Three infants were born alive, and 1 infant was stillborn; there were 7 pre-viable foetuses or lithopaedions, and 1 macerated foetus was born at 6 months. Of the 3 infants born alive 2 were delivered at term and 1 was born at the 8th month.

In 9 of the 12 patients the history suggested the diagnosis. Radiographs were taken in 10 cases; in 6 of these the extrauterine foetus was clearly shown. Transverse lie was common. A correct diagnosis was made pre-operatively in 7 cases. In 4 cases in which the placenta was removed, pregnancy was in the 4th or 5th month, the foetus was dead, and the placenta thrombosed and easy to separate. Of the other cases, in which the placenta was left intact, abscesses developed in 2. At the original operation neither drainage nor marsupialization was carried out.

There are three ways of dealing with the placenta at the primary operation: (1) by complete excision; (2) by marsupialization; (3) by non-intervention (the method of choice). The cord is ligated and cut close to the placenta. If the baby is dead and conditions permit, it is best to allow several weeks or months to elapse before operation so that the blood vessels can seal off and bleeding thus be minimized. *Lilian Raftery*

1862. **Primary Abdominal Pregnancy in the Lesser Peritoneal Cavity.**

By N. D. Elzey. *West. J. Surg. Obstet. Gynec.*, **56**, 410–413, July 1948. 53 refs.

LABOUR.

1863. **The Blood Picture in Labour and the Early Puerperium, in the Umbilical Cord, and in the Foetus at Term.** (Il quadro ematologico in travaglio di parto nei primi giorni di puerperio, nel funicolo ombellicale e nel neonato a termine.)

By G. Colucci and G. Vincenti. *Riv. ital. Ginec.*, **30**, 323–337, 1947. 38 refs.

Haematological examinations have been carried out on 20 healthy women in labour and in the first days of the puerperium, and on 20 newborn infants immediately after delivery and in the first days of life; in 7 of the infants the blood in the umbilical vessels was also examined. Delivery was physiological in 15 patients; 5 had a Caesarean section for contracted pelvis. Ten healthy non-pregnant women between the ages of 18 and 28 years and the same number of children between the ages of 2 and 6 years served as controls.

Results showed that there is no relation between the pictures of maternal and foetal blood, of maternal blood and cord blood, or of foetal blood and cord blood. Maternal oligocythaemia does not exist during labour, but there is a hypochromic anaemia, perhaps related to environmental, nutritional, and constitutional factors. A reduction in the number of erythrocytes was observed on the 2nd day of the puerperium compared with the number present during labour; this reduction was less apparent by the 4th day of the puerperium and the count became normal by the 8th day.

A polycythaemia exists in the foetus at term, and in 91 per cent of the cases the count increases until the 2nd day of life and then gradually decreases. A distinct anisocytosis and macrocytosis is present until the 24th hour of life. The erythrocyte count in the newborn infants appears to be always greater than that in the umbilical cord and in the mother in labour. Inversion of the leucocyte formula takes place on the 5th day of life and not on the second, as suggested by other workers. The authors believe that the trauma of normal labour does not cause polycythaemia in the newborn, since the blood counts of infants born after normal labour and of those delivered by Caesarean section were similar. The examination of blood from umbilical arteries and veins did not reveal differences. *Rina Saunders*

1864. **Nutrition, Serum Proteins, and the Quality of Contraction in Labour.** (Alimentación, protinemia y calidad de trabajo en el parto.)

By L. L. Mercado. *Obstet. Ginec. lat.-amer.*, **5**, 420–429, Sept. 1947. 6 refs.

The relation between the diet consumed during pregnancy and the nature of uterine action during labour has been investigated in 100 patients in Colombia. In 30 patients the diet consisted largely of maize, though in some cases meat and fish were consumed; in 35 patients the feeding was carried

out by the Inter-American Service of Public Health, and in 35 patients of the wealthy class the amount of protein was adequate and calcium and vitamins were added. The specific gravity of the blood and serum, and haemoglobin value and serum-protein level were estimated. The cases were classified in 3 groups according to the level of the serum proteins. In the 1st group of 20 patients, in whom the serum protein level was between 45 and 80 per cent of normal, the diet was largely a carbohydrate one, and a condition almost amounting to a " physiological diabetes of pregnancy " was found. In these patients there were excessive gain of weight, oedema, and slight hypertension, but lactation was found to be very good. Uterine action was unsatisfactory, and in 3 patients there was inertia. In 22 patients with serum protein levels between 80 and 90 per cent, uterine action was more satisfactory. In the 3rd group of 57 patients with serum protein levels between 90 and 110 per cent, uterine action was excellent. In these patients the diet was ample, and contained adequate milk, meat, fish, eggs, and cheese.

The author draws the provisional conclusions that an adequate amount of protein in the diet favours satisfactory uterine action in labour, and that while a defective diet with excess of carbohydrates produces oedema and slight hypertension, an adequate supply of carbohydrate helps lactation.

Bryan Williams

1865. **A Method of Induction of Labour.** (Un procedimiento para la inducción del parto.)

By E. VALENZUELA SAEZ. *Bol. Soc. chil. Obstet. Ginec.*, **12**, 97–108, July 1947. 10 refs.

The author reviews the usual methods of induction of labour, which fail in between 30 and 50 per cent of cases. A considerable foetal mortality has been reported with Aburel's method; in the author's experience one maternal death was associated with it, the actual cause of death being uncertain. [In the discussion on this paper, two speakers referred to the risks of Aburel's method.] The results are reported of the intravenous and intramuscular injection of a quinine-calcium preparation, together with artificial rupture of the membranes in some cases. [The composition of the quinine-calcium preparation is not stated.] In 8 cases in which the injections alone were given there were 4 failures, but in 12 cases in which the injections were followed by artificial rupture of the membranes there were no failures. The author considers the method to be free from risk for mother and baby.

Bryan Williams

1866. **Diagnosis and Treatment of Labour with Postmature Foetus.** (Zur Diagnose und Therapie der Spätgeburt.)

By H. HEBERER. *Geburtsh. u. Frauenheilk.*, **8**, 503–510, June 1948. 9 refs.

1867. **The Management of Prolonged Labour.**

By F. C. SPENCER. *Hawaii med. J.*, **7**, 389–391, May–June 1948.

1868. **Difficult and Delayed Labour.**

By D. N. HENDERSON. *Bull. Vancouver med. Ass.*, **24**, 267–272, May 1948.

1869. **The Management of Occipito Posterior Positions.**

By C. J. MCDEVITT. *Kentucky med. J.*, **46**, 269–271, July 1948.

1870. **Cervical Dystocia, with Special Reference to the Fibrous Nature of the Cervix.**

By O. H. SCHWARZ and R. B. WOOLF. *Amer. J. Obstet. Gynec.*, **55**, 151–168, Jan. 1948. 18 figs., 3 refs.

The authors of this article stress the fibrous nature of the cervix as the cause of functional rigidity in the elderly primipara. They state that annular detachment of the cervix takes place at the fibro-muscular junction. This was determined by the study of tissue from two such cases. It is asserted that amputation of the cervix leads to premature labour, because, when the fibrous part of the cervix is removed, there is no structure to keep the uterus from dilating. On the other hand, after conization of the cervix spontaneous delivery is not affected. The work of Danforth (*Amer. J. Obstet. Gynec.*, 1947, **53**, 541) on " the fibrous nature of the human cervix, and its relation to the isthmic segment in gravid and non-gravid uteri " is confirmed.

G. Gordon Lennon

1871. **Effect of a Sympathicolytic Drug on the Spastic Cervix.** (Wirkung eines Sympathikolytikum beim spastichen Muttermund.)

By H. SAUTER. *Gynaecologia, Basel*, **125**, 87–103, Jan.–Feb. 1948. 9 figs., 17 refs.

The author, who has carried out his research at the Women's Clinic of the University of Zürich, considers that the sympathetic nervous system innervates the cervix; he summarizes the literature on this most controversial subject.

Acting on his belief, he searched for a substance which, by inhibiting the sympathetic, would enable the cervix to dilate; he claims that yohimbine is such a substance. Its aphrodisiac action is due to dilatation of the pelvic blood vessels and relaxation of the pelvic musculature. Like ergotoxine it has two active components. The drug was used on 55 patients in labour, including 49 primiparae in whom signs of cervical rigidity, not responding to the usual sedatives and opiates, were present. This number was out of a total of 668 primiparae delivered in a period of 6 months. The dose was 0.01 g. orally or intramuscularly. A study of the lengthy case histories reveals that there were rapid softening, increase of elasticity, and dilatation of the hitherto inelastic cervix. An improvement in the type of pains was also claimed.

Delivery followed in most cases in from 4 to 8 hours after administration of the drug.

[In the discussion which followed this paper such authorities as Guggisberg of Berne and Frey of Zürich disputed the anatomical, physiological, and pharmacological basis of the experiments. The author had used a variety of other drugs in the series in which he claims success with yohimbine. It would seem worth while to attempt a properly controlled series of deliveries with spasmolytic drugs of this nature in cases of rigid cervix.]

Elliot E. Philipp

1872. **The Oxytocic Use of Methergine in the Third Stage of Labour.**

By J. E. TRITSCH, E. SCHNEIDER, and E. F. LONGWORTH. *N.Y. St. J. Med.*, **48**, 293–294, Feb. 1, 1948. 4 refs.

In a total of 911 cases " methergine " (methylergometrine) was given intravenously to 810 patients and intramuscularly to 101 patients in the third stage of labour in doses of 1 ml. containing 0.2 mg. No toxic effects were observed. Postpartum blood loss was apparently reduced, an average of 115 ml. being lost after intravenous administration. Manual removal of the placenta was necessary in 7 cases.

S. S. B. Gilder

1873. **The Intrauterine Pack in the Management of Postpartum Haemorrhage.**

By L. A. DAY, R. D. MUSSEY, and R. W. DEVOE. *Amer. J. Obstet. Gynec.*, **55**, 231–243, Feb. 1948. 23 refs.

In this paper from the Mayo Clinic the authors review the literature on the use of the intrauterine pack in the management of postpartum haemorrhage. Some authors condemn the employment of the pack, alleging that it prevents uterine retraction and that a haemorrhage that would otherwise be revealed is converted into a concealed one. Others say that the pack should be used as soon as it becomes evident that haemorrhage is not being controlled by the usual measures. If bleeding continues after delivery of the placenta and is not controlled by massage of the fundus and intramuscular or preferably intravenous administration of ergot the authors pack the uterus with sterile gauze, using a packing forceps. In cases of severe bleeding from an atonic uterus the vagina is also tightly packed. When the delivery has been complicated by placenta praevia, uterine and vaginal packs are usually inserted as a precautionary measure even though bleeding is not pronounced. Uterine tamponade has been employed in the Mayo Clinic since 1918. In 12,000 deliveries it was used 267 times. Not only is it used in cases of haemorrhage but also as a prophylactic after manual removal of the placenta when the uterus is atonic and firm contraction is not induced by other methods. Six of the patients continued to bleed through the pack but the bleeding was controlled by re-packing in 3 of the cases. In the other 3 it was not controlled and hysterectomy had to be performed. In one of these cases there was a marginal placenta praevia. The morbidity rate was not any higher among the patients in whom a pack had been inserted than among other patients with anaemia after postpartum haemorrhage. One patient, however, died on the 8th day of the puerperium, apparently from a haemolytic streptococcal infection in the days before chemotherapy. The authors conclude that the pack has a definite place in the management of postpartum haemorrhage.

In the discussion that followed this paper opinion was about equally divided on the value of packing. Some condemned it as being unnecessary in the less severe cases and futile in the more severe ones. It was pointed out by Bill of Chicago that often a few minutes after firm packing the uterus will relax and fill with blood behind the pack. [This would seem to be the chief objection to the method —that the uterus is alternately contracting and relaxing and that it is therefore impossible to be sure of fulfilling the essential purpose of the pack, to exert *continuous* pressure on the bleeding point.]

F. J. Browne

1874. **The Dosage of " Methergine ".** (Ueber die Dosierung von Methergin.)

By H. SAUTER. *Schweiz. med. Wschr.*, **78**, 162–163, Feb. 21, 1948. 5 figs., 4 refs.

Tonometric investigations and clinical observations confirmed the fact that the dose of " methergine " (methylergometrine) employed at present (1 to 2 ml. or 0.2 to 0.4 mg.) is too high for the treatment of postpartum haemorrhage due to atony. The maximal and most prolonged contractions can be achieved with 0.25 ml. of methergine.

Harold Jarvis

1875. **Fatal Hemorrhage Associated with the Third Stage of Labor. A Study of 60 Maternal Deaths, Brooklyn 1937–1947.**

By M. GLASS and A. H. ROSENTHAL. *N.Y. St. J. Med.*, **48**, 159–165, Jan. 15, 1948. 9 refs.

Sixty cases of death from haemorrhage in the third stage of labour are reviewed; the causes of haemorrhage were: (1) atony of uterus, 40 cases; (2) retention of placenta, 12 cases; (3) inversion of uterus, 5 cases; (4) varied causes, 3 cases.

(1) *Atony of the uterus.* Ten patients with premature separation of a normally implanted placenta died of postpartum haemorrhage superimposed upon antepartum or intrapartum bleeding. In 6 vaginal deliveries the placenta was delivered more half an hour after the child, and manual removal was required in 3 cases. Fibroids, prolonged labour, and over-distension were all predisposing factors. So, according to the authors, was general anaesthesia. (2) *Retention of the placenta.* Twelve fatal haemorrhages were associated with retention of placental tissue; 5 of the patients died with the placenta completely retained. One woman died in

hospital 36 hours after a normal delivery, having been returned to bed with the placenta retained. (3) *Inversion of the uterus.* Manual expression of the placenta with or without traction on the cord accounted for 4 of the 5 recorded cases.

Forty-one patients died within 5 hours of delivery, 29 being dead within 3 hours. In 80 per cent of the cases either no blood or an insufficient amount of blood was given. A strong plea is made for prenatal blood grouping and determination of the Rh factor. The uterine pack is advocated, although it was used unsuccessfully in 31 of the cases analyzed. In some cases of uterine atony the placenta was allowed to remain in the uterus for more than 1 hour despite a blood loss exceeding 1,000 ml. In the majority of cases the period between haemorrhage and death, though brief, was sufficient for adequate blood replacement to have been carried out. Four cases of inversion of the uterus occurred because of mismanagement of the third stage.

[This article is a salutary reminder of the heavy maternal mortality arising from mismanagement of the third stage of labour and of the need for: (1) adequate antenatal supervision so that anaemia may be corrected and blood and Rh group determined, and (2) provision of adequate facilities for rapid blood transfusion.] *Leslie A. Cruttenden*

1876. **Haemorrhage in Obstetrics: the Relation Between the General Practitioner and Emergency Services.**

By R. E. SOLDENHOFF. *Edinb. med. J.*, **55**, 302–315, May 1948. 6 refs.

ANAESTHESIA.

1877. **A New Apparatus for Obstetric Analgesia.** (Et Nyt Obstetrisk Analgesi-apparat.)

By E. T. MØRCH. *Ugeskr. Laeg.*, **30**, 856–857, July 22, 1948. 1 fig.

1878. **Comparative Study of Three Methods of Anaesthesia and Analgesia in Obstetrics.** (Estudio comparativo de tres metodos de analgesia y anestesia en obstetricia.)

By G. A. DE LA VEGA, R. GARCIA ROEL, M. MARISCAL, and R. BRISENO. *Rev. méd. Hosp. gen.*, **11**, 241–252, Apr. 1948. 11 refs.

1879. **Intravenous "Recorcain" (Procaine) Analgesia in Labour.** (Analgesia in travaglio di parto con recorcaina endovenosa.)

By A. SALVINI and F. FERRERO. *Riv. ital. Ginec.*, **30**, 397–407, 1947. 8 refs.

The authors have studied the production of analgesia in labour by intravenous injections of 1 per cent procaine in 5 per cent glucose solution. Of the 10 women treated 5 were primigravidae and 5 multigravidae. The drug was always given during the second stage of labour at an average rate of 4 to 8 ml. per minute; as little as 70 ml. in some cases and as much as 232 ml. in others was found necessary. The average time required to obtain analgesia was 5 to 10 minutes. Before commencing the injection 1 drop was introduced intramuscularly; blood pressure, pulse rate, respiration rate, and foetal heart rate were observed during the treatment. In each experiment a few ml. per minute was first given and the dosage was increased or decreased according to the local and general reaction obtained in each case; care was taken to avoid too deep a central action of the drug.

The results were very good in 5 cases, good in 3, and poor in 2. During the treatment the patients appeared sleepy and semi-conscious and talked incoherently, but most of them were able to answer questions. In 1 case, soon after the administration began, the patient had a convulsion and became cyanotic and dyspnoeic with a rapid pulse rate; the injection was discontinued and after treatment with artificial respiration, lobeline, and camphor the patient recovered quickly; the injection was not resumed and she had a normal delivery without pain. In 2 other cases convulsive movements began and the injection was discontinued for a few minutes and resumed soon after the patient had recovered. Forceps were used twice because the uterine contractions became weak and there were signs of foetal distress. In all other cases the uterine contractions were unaltered; all the patients were able to bear down during the expulsive period and amnesia is reported in most cases. All the babies were born alive with no signs of distress. The analgesic effect was maintained for some time after delivery. The authors consider their results encouraging, but further study of the method is needed. *Rina Saunders*

1880. **Paraldehyde and Barbiturate Analgesia in Labour.**

By R. MACKEY. *Med. J. Aust.*, **2**, 748–750, Dec. 20, 1947.

"Seconal" (sodium allyl (1-methylbutyl) barbiturate) was used in conjunction with paraldehyde to produce analgesia and amnesia in labour. Two capsules (3 g.) of seconal were given as soon as the patient went into labour or on her admission to the labour ward. This was followed in 10 to 15 minutes by oral administration of 6 frozen capsules of paraldehyde, each capsule containing 17 minims (1 ml.). The importance of administering the paraldehyde regardless of the initial effect of the seconal is emphasized. A further 2 capsules of paraldehyde were given if the patient woke up between the uterine contractions. On this basis it was found necessary to give paraldehyde capsules almost every hour, not more than 20 capsules being given to any one patient; 279 patients were treated. In 86.7 per cent of cases analgesia and amnesia were complete or almost complete. The sedation was

unsuccessful in 4.7 per cent and unsatisfactory in 8.6 per cent of cases. The average duration of analgesia was 6 hours 22 minutes. The longest period was 27 hours 25 minutes. Labour was not prolonged in any of its stages. The incidence of forceps delivery in primigravidae was 35 per cent and in multiparae 17 per cent. Postpartum haemorrhage, defined as blood loss greater than 20 oz. (568 ml.), occurred in 29 patients—an incidence of 12.4 per cent. There was no increase in foetal or neonatal death rates, or in maternal mortality or morbidity. *T. N. MacGregor*

1881. **" Nupercaine " Spinal Anaesthesia in Obstetrics. (Report of 100 Cases.)**

By J. T. HUGILL and C. GILLESPIE. *Canad. med. Ass. J.*, **58**, 146–149, Feb. 1948. 12 refs.

The authors describe a method of low spinal analgesia with 1 in 200 heavy " nupercaine " for use in obstetrics. This drug is used to alleviate pain in the latter part of the first stage, and during the second stage of labour. Relief of pain lasts for 4 to 8 hours and operative procedures may be carried out *per vaginum* with the minimum of inhalation anaesthesia. A series of 100 cases where spinal analgesia was employed is compared with a similar series in which gas–oxygen–ether was the anaesthetic. No serious complications due to the analgesic were encountered, but there was an increase in the forceps rate and in the incidence of posterior positions of the occiput. On the other hand, postpartum haemorrhage was less common, and fewer of the children required resuscitation. The authors stress that spinal analgesia is only suitable in institutions where skilled anaesthetists are available. *D. M. Sheppard*

1882. **Spinal Anesthesia in More Than Five Thousand Vaginal Deliveries.**

By W. C. ROGERS. *West. J. Surg. Obstet. Gynec.*, **56**, 236–242, Apr. 1948. 7 refs.

1883. **Newborn Mortality and Morbidity with Continuous Caudal Analgesia. An Analysis of Cases in New York, Philadelphia and Memphis, with Controls.**

By R. A. HINGSON, W. B. EDWARDS, C. B. LULL, F. E. WHITACRE, and H. C. FRANKLIN. *J. Amer. med. Ass.*, **136**, 221–229, Jan. 24, 1948. 8 figs., 3 refs.

The authors claim to have demonstrated clearly that all forms of regional nerve-block analgesia for labour reduce infant mortality; they have compared their results with control groups managed with systemic narcosis, general anaesthesia, or no anaesthesia. These methods of nerve-conduction analgesia include local, pudenal and presacral-block, spinal, saddle-block spinal, caudal, and continuous caudal analgesia. This study is primarily concerned with the last-named method, and groups of patients treated in this way are compared with control groups.

In all 7,893 births have been studied, 5,059 of which were managed with continuous caudal analgesia and 2,834 with other methods, including a group of 577 in which no anaesthesia whatever was given. These cases were derived from the U.S. Marine Hospital, New York, the Philadelphia Lying-In Hospital, and the John Gaston Hospital, Memphis, Tenn. These studies all show a considerably lower mortality rate, including both stillbirths and neonatal deaths, when continuous caudal analgesia was given, in spite of the following dangers of the method: (1) Primary intrauterine foetal anoxia resulting from hypotension due to the nerve block of vaso-motor nerves. (2) Arrested or prolonged labours following too early induction of analgesia or extension of anaesthetic levels above the sixth thoracic segment or through the anterior sacral foramina to Frankenhäuser's ganglia. (3) Increased incidence of occipito-posterior positions. (4) Increased incidence of operative deliveries. (5) Occasional transplacental foetal hypersensitivity to the analgesic agent used.

In the New York study the total mortality with caudal analgesia (more or less equally divided between stillbirths and neonatal deaths) was 16.2 per 1,000 live births, as against a figure of 28.3 per 1,000 for spinal analgesia and 162.2 per 1,000 for births in which no anaesthetic was used. The higher rate in patients receiving spinal analgesia is explained by the marked fall in blood pressure which often occurred. In Philadelphia, with caudal analgesia the death rate was 20.6 per 1,000 compared with 45.6 in the control group where gas-oxygen–ether was the principal anaesthetic method used. It is stressed that the mothers in the 2 groups were strictly comparable as regards age, parity, and other factors affecting labour. In Memphis, where negroes outnumbered whites by 2 to 1, the total mortality was 36.8 per 1,000 live births with caudal analgesia, 74.2 with spinal analgesia, 73.2 with general anaesthesia, and 144 in the large group of 577 cases receiving no anaesthetic. It is pointed out that the higher figures in all groups in this study are probably associated with the greater tendency to stillbirths and neonatal deaths in negroes. Difficulty was experienced in establishing respiration in only 3.6 per cent of infants who survived in the caudal analgesia group compared with 9.6 per cent of infants surviving in the control group. In the caudal analgesia series 11.9 per cent of infants had a net weight gain the first week compared with 9.2 per cent of the control group. More favourable results for caudal analgesia were consistently seen when the groups were broken down into age groups and when premature and mature infants were separated. For purposes of comparison all infants of under 3 lb. (1.35 kg.) weight were excluded from the study, as this would have loaded unfavourably the group not receiving anaesthesia.

The strikingly high figures in both the New York

and the Memphis studies for the group receiving no anaesthesia emphasize the dangers of " uncontrolled tumultuous labour as a cause of anoxia and pressure trauma of the rigid maternal musculature against the soft tissues of the infant," especially where there is voluntary muscular straining. Consequently the authors question the safety for the infant of methods that withhold relief during labour and delivery. [It may be noted that in these cases many deliveries were precipitate or " occurred at times when all available intern and residency supervision was utilized in the delivery of other patients " so that the figures for the group receiving no anaesthesia tend to be unfavourably weighted.]
J. A. Chalmers

1884. **Infiltration during Labour of Lumbar Sympathetic with Analgesics of Prolonged Action.** (Anesthesiques-retard dans les infiltrations analgésiques du sympathique lombaire au cours du travail.)

By H. PIGEAUD and R. GARMIER. *Rev. franç. Gynéc.*, **43**, 210–212, June 1948. 9 refs.

PUERPERIUM.

1885. **Puerperal Inversion of the Uterus and its Spontaneous Reinversion.** (Puerperální děložní inverse se spontánní reinversí.)

By J. SYNEK. *Ceskoslov. Gynaek.*, **13**, 76–80, 1948. 9 refs.

The case is described of a 37-year-old 3-gravida who, after a pregnancy complicated by mild toxaemia in the last month, had a normal delivery at term. On the sixth day after delivery the uterus became inverted, without evident cause. A careful attempt at reposition failed; further attempts were considered inadvisable, at first because of the shock, later because of a severe anaemia (though there had been no bleeding), and still later because of a recurring thrombophlebitis of both legs. An examination 16 weeks after the inversion, and 5 weeks after the patient had last been examined, revealed a normal uterus. The author thinks that the inversion was caused by the presence of a few small myomata in the anterior wall of the uterus, and the exhaustion of the organism by the toxaemia of pregnancy (which probably also caused the severe anaemia). The restitution of the general condition was accompanied by spontaneous reinversion.
A. Rohan

1886. **Penicillin Vaginal Suppositories and the Prevention of Post-partum Morbidity.**

By R. R. PIERCE. *Amer. J. Obstet. Gynec.*, **55**, 313–315, Feb. 1948.

A total of 1,573 patients was delivered at the Cincinnati General Hospital from July 1946 to March 1947. Alternate patients (778) received 200,000 units of penicillin in cocoa-butter suppositories, which were inserted in the posterior fornix of the vagina with sponge forceps immediately after delivery. The other 795 cases served as controls. Of the 778 patients who received penicillin 18 or 2.3 per cent developed genital-tract infection. There were 42 cases of genital tract infection among the controls, an incidence of 5.3 per cent.

Levels of penicillin in the blood were determined in 49 patients; in 38 the levels averaged 0.06 unit per ml. of serum in half an hour, 0.06 to 0.25 unit at 1 hour, and 0.06 to 1 unit in 2 hours. The absorption of penicillin seemed to depend on the amount of bleeding postpartum.

[The nature of the organisms causing the puerperal infection is not stated.] *D. M. Stern*

1887. **Treatment of Puerperal Mastitis with Penicillin.** (Uber die Behandlung der Mastitis puerperalis mit Penicillin.)

By W. NEUWEILER. *Praxis.*, **37**, 21–23, Jan. 15, 1948. 5 refs.

In cases of puerperal mastitis at the University Maternity Hospital, Berne, 50,000 to 80,000 international units of crystalline sodium penicillin in 10 to 20 ml. normal saline solution are injected into the inflamed area in two places. After the injection an ice-bag is placed over the breast. The injection is given daily for 5 to 7 days. A day or two after the first injection the inflammation starts to subside—the area becomes smaller, very firm but painless, and subsides slowly after 14 days. The resorption of this firm mass is hastened by the application of heat. If there is an abscess when the patient is first seen, similar treatment is given, but in addition a small puncture is made, as much pus as possible is evacuated, and the abscess cavity is filled with penicillin. The maximum dose of 80,000 units is given in these cases. The abscess is only opened widely if the pus is thick and cannot be aspirated. In the early days of penicillin treatment of mastitis intramuscular injections were also given but the results were no better.

Kastle has shown that penicillin is not excreted in recognizable amounts in the milk. In the majority of cases of puerperal mastitis the infection spreads slowly along the milk ducts, hence if there is no penicillin in the ducts after intramuscular injection its use appears to be valueless. In cows puerperal mastitis is successfully treated by injection of penicillin to the milk duct, but this treatment is not feasible in women because of the large number of milk ducts opening on the nipple. The author investigated the growth of organisms in the milk of patients with mastitis who were treated by intramuscular injection of penicillin; doses of 200,000 units did not inhibit their growth, but intramammary injections of 50,000 to 80,000 units inhibited the growth—80,000 completely, 50,000 less effectively, and 30,000 not at all.

After local mammary injections only relatively small quantities of penicillin in a few cases passed over into the milk.
Gladys Dodds

1888. **Cure of 3 Cases of Puerperal Infection Due to** *Clostridium perfringens*. (Trois cas de guérison de septicémies puerpérales à perfringens.)

By P. TRILLAT *and A.* NOTTER. *Rev. franç. Gynéc.*, **43**, 225–234, June 1948. 28 refs.

LACTATION.

1889. **The Value of Ethinyl-Oestradiol in the Inhibition of Lactation.** (El valor del etinil-estradiol como inhibidor de la secreción láctea.)

By R. M. GORI and E. BAYONA. *Obstet. Ginec. lat.-amer.*, **5**, 448–495, Oct. 31, 1947. 32 refs.

Reports in the literature show that both the natural and synthetic oestrogens when given in adequate doses inhibit lactation, and some authors have also given progesterone and the androgens for the same purpose. There have been few reports on the use in the puerperium of ethinyl-oestradiol, which is a powerful oestrogen having a potency similar to that of oestradiol when administered by injection, but which is 15 to 20 times more effective when given by mouth. Good results have been reported by one author with doses of between 0.5 and 4 mg., and by others with a daily dose of between 1.8 and 2.4 mg. for 3 days.

The results are reported in 68 patients in the puerperium whose babies had been stillborn or had died. In nearly all of them breast development was satisfactory or there was a history of previous successful lactation. In 22 patients varying doses were given to find the optimum amount. It was found that a total of 3 mg. was satisfactory; an initial dose of 0.6 mg. was followed by daily doses of 0.5, 0.5, 0.4, 0.4, 0.3, 0.2, and 0.1 mg. In 25 patients given this amount there were only 2 failures. Administration must be started within 48 hours of delivery. No other treatment is necessary, and tolerance is good.

The factor of suction was investigated in 7 patients; babies of mothers who had not received the drug were put to the breast of mothers who had been given the drug, but they obtained little milk, and no milk could be obtained by manual expression. In 14 other patients an electric extractor was used on several occasions with similar results; the largest amount obtained was 70 ml. in 1 day. The one failure in this series occurred in a case in which treatment was started only when milk secretion was profuse, and in which administration of the drug had to be discontinued on account of intolerance.

The authors consider that ethinyl-oestradiol is a satisfactory drug in 90 per cent of cases, when given early and in moderate doses, for preventing breast engorgement and milk secretion.

Bryan Williams

1890. **Inhibition of Lactation by Male Sex Hormone.** (Inhibition de la secrétion lactée par l'hormone mâle.)

By M. DUMONT. *Rev. franç. Gynéc.*, **43**, 213–217, June 1948. 15 refs.

1891. **Breast Reduction and Lactation.**

By A. RAGNELL. *Brit. J. plast. Surg.*, **1**, 99–103, July 1948. 3 figs., 1 ref.

THE INFANT.

1892. **The Heart in Normal Infants and Children. Incidence of Precordial Systolic Murmurs and Fluoroscopic and Electrocardiographic Studies.**

By N. EPSTEIN. *J. Pediat.*, **32**, 39–45, Jan. 1948. 1 fig., 12 refs.

This paper records the clinical, radiological, and electrocardiographic findings in a group of 260 presumably normal children, varying in age from birth to 14 years. Each child was examined at least 4 times a year, and the average duration of observation was about 5 years. Over 50 per cent of the children who were under 7 years of age had systolic murmurs, and a murmur was audible in 66 per cent of the children between the ages of 8 and 14 years. Radiological examination in the posterio-anterior position showed that the heart was normal in shape in all cases. In the right anterior oblique position none of the patients revealed evidence of enlargement of the left ventricle. On the other hand, in the left anterior oblique position the angle of clearance of the left ventricle was 50 degrees ± in 90 per cent of the children. No statistical differences were obtained by comparison of the electrocardiograms of children with and without murmurs at various age levels. In about 18 per cent of the patients there were sporadic electrocardiographic abnormalities. *Jas. M. Smellie*

1893. **Resuscitation Unit in the Leonar Mendez de Barros Hospital for Mothers and Babies.** (Servicio de reanimación de la casa maternal e da infancia "Leonor Mendez de Barros".)

By E. MENDOZA, A. R. MARTÍNEZ, and J. C. SOARES BICUDO. *Obstet. Ginec. lat.-amer.*, **5**, 483–488, Oct. 31, 1947. 1 fig., 18 refs.

A unit for the resuscitation of the newborn is described, together with the technique used and the results. The unit is next to the labour ward, and the table where the baby is resuscitated is warmed with electric bulbs, the degree of heat being adjustable. An Emerson apparatus for artificial respiration is used. Gentleness in the treatment of asphyxia in the newborn is essential, and violent methods such as those of Silvester and Schultz are avoided. In cases where cerebral haemorrhage is suspected the head is kept slightly raised, but in all others the head is kept below the level of the body, to allow mucus to drain from the respiratory passages. Endotracheal aspiration by means of a laryngoscope is carried out where possible, but otherwise the pharynx is cleared. Oxygen is insufflated, and the baby is subsequently placed in a Hess incubator. α-Lobeline is sometimes given, but is not considered essential.

In one year resuscitation was carried out 166 times in 3,232 deliveries. In 24 atonic babies the object of treatment was to prevent neonatal complications; the results were satisfactory in all. In 70 cases of slight asphyxia lasting less than 5 minutes there were 5 neonatal deaths; in 35 cases of moderate asphyxia lasting 5 to 10 minutes there were 6 neonatal deaths; and in 23 cases of severe asphyxia lasting more than 10 minutes there were 7 deaths during resuscitation and four deaths later; all the babies who died during resuscitation were found at necropsy to have lesions incompatible with life. In 5 cases resuscitation was attempted although there were no heart sounds at birth.

In all cases the treatment was started within 1 minute after delivery. In none of the babies who died after a few days were there any lesions which could be attributed to the Emerson apparatus. The highest incidence of asphyxiation occurred during delivery of the after-coming head. The authors conclude that every labour ward should possess a resuscitation unit. Their methods, which should, they consider, be employed even in cases of slight asphyxia, have been successful in 92.78 per cent of cases, with a final viability rate of 83.73 per cent. *Bryan Williams*

1894. **Congenital Esophageal Atresia and Tracheo-esophageal Fistula.**

By C. G. LYON and S. G. JOHNSON. *J. thorac. surg.*, **17**, 162–177, Apr. 1948. 2 figs., 9 refs.

In a recent review of the literature the authors have been able to find reports of 468 cases of oesophageal atresia with or without tracheo-oesophageal fistula. They tabulate and give diagrams of the types of anomaly reported in 3 large series of cases. They then report 4 cases upon which they operated at the University of California Hospital. Intratracheal ether and oxygen was administered and the left transpleural approach was used in all 4 cases. The pleural space was entered through the bed of the fifth rib. The first patient was operated upon at the age of 60 hours. A blind upper oesophageal segment and a short blind lower segment were found, neither of them having a communication with the trachea. The diaphragm was opened and an oesophago-gastric anastomosis was made just above the level of the arch of the aorta after resecting the lower end of the oesophagus and a portion of the stomach. The child developed aspiration pneumonia from regurgitating a feed and died 48 hours after operation. At necropsy, the anastomosis appeared viable.

The second patient was operated upon 120 hours after birth. A blind upper segment was encountered, and a lower segment having a fistulous communication with the trachea. The fistula was separated, ligated, and divided and an anastomosis made between the upper and lower segments of the oesophagus, after rotating the distal segment 180 degrees, as suggested by Gross. The child died 19½ hours afterwards of extensive bilateral pneumonia. The anastomosis admitted nothing larger than 2.5 mm. probe.

The third patient was operated on at the age of 88 hours. A blind upper oesophageal segment and a lower segment communicating with the trachea were revealed. After separation of the fistula, the upper and lower segments were anastomosed end-to-end. The postoperative course was complicated by a reopening of the tracheal fistula, and the development of a stricture at the site of anastomosis. In spite of dilatation of the stricture the patient died. Necropsy revealed a small abscess around the anastomosis, with re-opening of the tracheal fistula. In addition there was a second area of stenosis of the lower oesophageal segment 2 cm. distal to the fistula. The lungs showed bilateral pneumonia and atelectasis.

The fourth infant was operated on at 36 hours of age. Previous investigation with " lipiodol " had disclosed a blind upper oesophageal segment and a lower oesophageal segment, which communicated with the trachea. The oesophago-tracheal fistula was obliterated and the upper and lower oesophageal segments were united by end-to-end anastomosis. The child was discharged 23 days after entry in excellent condition. She takes fluid readily, but purées must be diluted, and dilatation may be required in the future.

In the 3 cases of end-to-end anastomosis a transverse opening was made in the most dependent portion of the upper oesophageal segment and a longitudinal incision of comparable length in the lower segment. The segments were anastomosed with 2 rows of ooooo " deknatel " sutures. Interrupted sutures were used to approximate the mucosa, and mattress sutures to approximate the muscularis. *Hugh Reid*

1895. **A Simultaneous Abdominal and Perineal Approach in Operations for Imperforate Anus with Atresia of the Rectum and Rectosigmoid.**

By J. E. RHOADS, R. L. PIPES, and J. PERLINGIERO RANDALL. *Ann. Surg.*, **127**, 552–556, Mar. 1948. 4 figs., 7 refs.

A one-stage abdomino-perineal operation is suggested for certain cases of imperforate anus in which the colon cannot be reached safely from the perineum. The operation is facilitated by preparing the skin of the entire baby from the axillae to the toes so that the two approaches can be used simultaneously. Two cases are reported, one child surviving 3 months, at which time he succumbed with uraemia, and the other surviving and healthy at 8 months of age.—[Authors' conclusions.]

1896. **Acute Intussusception in Childhood.**

By B. MORRISON and D. COURT. *Brit. med. J.*, **1**, 776–780, Apr. 24, 1948. 1 fig., 8 refs.

A careful study has been made of 100 children treated for acute intussusception over a 2-year

period in the Department of Child Health, Newcastle-upon-Tyne. Of these children 66 were seen by their own doctor within the first 24 hours, but only 34 were admitted to hospital within that period; in at least 17 cases, and probably in more—for the time interval was not known in all of them—the child was not admitted to hospital until after the end of the second day, and in some cases the delay was for as long as 7 days. The total fatality rate was 10 per cent, that for the children treated within the first 24 hours 5 per cent, and that for children treated after 48 hours 20 per cent or more.

Most children were between 3 and 9 months old, and 82 of the patients were under 1 year. Male preponderance was less in this than in some previous series, and the sex ratio was only 11:9. Most of the children were well-nourished, as in the series of previous authors, but precipitating factors did not bulk large in the series. Unwise dietetics could not be blamed in the majority of cases, and the actual process of weaning had been recently begun only in 29 per cent of cases. In 10 of the children a period of a few days' malaise preceded the intussusception and sometimes tended to obscure the diagnosis. A study of the actual clinical features bears out the accepted textbook picture of the disease, but vomiting was rather more frequent than it is commonly believed to be, occurring in 88 per cent. A tumour was felt in 88 per cent. It was considered that in previous series some deaths attributed to surgical intervention were, in fact, due to uncorrected circulatory failure. Special pains were therefore taken to transfuse adequately, 100 ml. of serum or plasma being given initially to a child under 9 months old, and 150 ml. to a child between 9 and 18 months old; saline was given later if required.

The treatment was in all cases operative. After studying the previous series in which enemata had been used alone or in combination with operation, the authors deduced that the success of enemata in these was due to the high proportion of early cases seen, rather than to any advantage which enemata have over operation. Comparing their series with the previous series of Hipsley, Nordentoft and Nyborg, all of whom advocated enemata, they see no reason to prefer enema administration to their present operative regimen. *Ian Aird*

1897. **Acute Intussusception in Infancy and Childhood.**

By W. M. DENNISON. *Glasg. med. J.*, **29**, 71–80, Mar. 1948. 15 refs.

This article describes the management of acute intussusception as practised by surgeons of one unit at the Royal Hospital for Sick Children, Glasgow; 237 patients have been treated over a period of 10 years and an analysis of these cases is presented. The author's views upon the treatment of the irreducible intussusception are of particular interest. In all, 14 such cases were treated, 9 by resection with 5 deaths, and 5 by lateral anastomosis with 1 death. The successful outcome in 4 cases of simple lateral anastomosis without resection has suggested to the author that this method may be preferable to resection as a treatment in these cases. The author considers that death in cases of non-reduced intussusception is usually due to intestinal obstruction and that peritonitis is a rare cause of death. Although the intussusception may be gangrenous, the ensheathing layer is almost invariably viable. Therefore lateral anastomosis is a satisfactory procedure and the gangrenous inner layers are passed as a slough some days later.

C. G. Rob

1898. **Clinical Statistics of Empyema in Infancy over a 15-Year Period (1931–47).** (Considerazioni statistico-cliniche sulla pleurite purulenta dell'infanzia nel corso di un quindicennio (1931–1947).)

By U. GIURANNA and C. MELINO. *Pediatria*, **56**, 48–63, Jan.–Mar. 1948. 5 figs., 33 refs.

In the years before sulphonamides were used, 1931–38, the incidence of empyema in the Paediatric Clinic of the University of Naples was 2.1 per cent. From 1938 to 1947 it was 0.31 per cent, the actual number of cases being 580 out of 60,780. The incidence of empyema due to broncho-pneumonia was 40 per cent up to 1938, and 14.9 per cent afterwards. This fall was parallel to the diminution in the number of cases of acute respiratory disease reported to the health authorities, from 55,000 in 1939 to 35,000 in 1946. The organisms chiefly responsible were pneumococci (77 per cent and 72.9 per cent), staphylococci and streptococci occurring much more rarely. The greatest incidence was in the second year of life; this was equally true of staphylococcal cases, an observation not recorded by other workers. The figures for streptococcal infections are too small to be significant. The relative incidence of para-pneumonic and meta-pneumonic empyemas is unchanged, nor is the recovery rate much altered, being slightly greater in the later series in the para-pneumonic types—67.7 per cent against 58.9 per cent. The rate in meta-pneumonic infections is approximately 78.0 per cent. The right and the left side were equally involved.

[This last statement is associated by the author with the figures for the incidence of broncho-pneumonia in the right and left lungs, these figures also revealing an equal incidence. Presumably the definition of broncho-pneumonia is not the same as in Britain.] *J. G. Jamieson*

1899. **Penicillin Therapy in Infantile Empyema.** (Ulteriore contributo alla terapia penicillinica nell' empiema pleurico dell'infanzia.)

By G. MURANO. *Pediatria*, **55**, 563–591, July–Sept. 1947. 17 figs., bibliography.

Attention is drawn to the greatly diminished morbidity from empyema in childhood from 1938

onwards, because of the use of sulphonamides in acute respiratory infections. Between the years 1932 and 1938 cases of empyema formed 2.78 per cent of all admissions to the wards of the children's clinic in Naples, but only 1.44 per cent between 1940 and 1946; in the out-patient department, the incidence of empyema fell from 2.19 to 0.26 per cent. The mortality rate rose, however, because a greater proportion of cases were staphylococcal. Even with the use of penicillin the prognosis of infantile empyema is still not good, mainly because of the development of pleural thickening. The author records a series of 19 cases in detail, all treated with intrapleural and systemic penicillin. The pleural cavity was aspirated every 2 or 3 days and 15,000 to 30,000 units of penicillin were instilled; between aspirations 10 ml. of 10 per cent sodium taurocholate or 3 per cent quinine hydrochloride solution was injected in order to liquefy the pus. It is claimed that the frequency of thoracotomy is thereby greatly reduced. Only in 3 cases was open drainage performed, pus was evacuated in one case; the other two merely had thickened and organized pleura. A third of the empyemata were staphylococcal, and 13 of the 19 patients were under 2 years of age. The average length of stay in hospital was 20 to 30 days instead of 2 months as formerly. Two children died, both of pyaemia, shortly after admission. Penicillin did not prevent the development of considerable pleural thickening, and the author suggests the use of intrapleural heparin as early as possible in treatment to prevent the deposition of fibrin.

E. G. Sita-Lumsden

1900. **Suppurative Meningitis in the Newborn Due to Coliform Bacilli.**

By K. J. RANDALL. *J. clin. Path.*, **1**, 150–155, May 1948. 2 figs., 15 refs.

Although infrequent, suppurative meningitis in the first month of life is now more commonly recognized than formerly. This paper reports 6 cases of meningitis due to coliform bacilli. The ages of the infants ranged from 17 hours to 16 days and 2 of them were premature. The signs and symptoms are not typically those of meningitis; the temperature may be normal, but a sudden rise in temperature was an early sign in 4 of these cases. Other early signs are a failure to feed, restlessness, twitching of the limbs, and muscular spasms, but neck rigidity is rare. Convulsions often occur before death and a cephalic cry may develop. The author remarks that these signs are suggestive of an intracranial lesion or at any rate of cerebral anoxia, and urges an early examination of the cerebrospinal fluid. All these cases were due to *Bacterium coli*; a review of the literature shows this to be the commonest organism causing meningitis at this age. There is some evidence to suggest that the newborn may lack the normal coli agglutinins present in adults. In only one case was any specific treatment (sulphathiazole) given; this was without effect. In one case the organism was sensitive to 100 units of penicillin per ml. *N. S. Alcock*

1901. **Etiological Aspects of Gastroenteritis. Parts I and II.**

By E. HINDEN. *Arch. Dis. Childh.*, **23**, 27–39, Mar. 1948. 1 fig., bibliography.

A series of 148 cases of gastro-enteritis in infants were treated in the County Hospital, Kensington, in 24 months from April, 1938. The mortality rate was 44 per cent. The mortality rate in the 88 infants admitted with gastro-enteritis was 31 per cent and in the 60 who acquired it in hospital it was 63 per cent.

[Only two aspects of treatment are discussed—chemotherapy and the use of blood products. An important omission is a discussion of the common errors of nursery technique which invite epidemics of gastro-enteritis.] *R. S. Illingworth*

1902. **Intravenous Procaine in the Treatment of Toxaemic Syndromes in the Infant.** (La novocaina endovenosa nel trattamento delle sindromi tossiche del lattante.)

By E. SORAGNI. *Clin. pediat., Bologna*, **30**, 45–54, Jan. 1948. 34 refs.

The author discusses the use of intravenous procaine in the treatment of 18 cases of gastro-enteritis with toxaemia, in the University of Modena. One patient was 3 years old, while all the others were between 15 days and 12 months old. In 11 cases the cause was primarily intestinal, while in the remaining 7 cases there was a parenteral infection. In all cases there was diarrhoea, vomiting, dehydration, and a toxic facies, and in addition most children had albuminuria and pyrexia. The procaine (1 per cent solution) was injected into the longitudinal sinus or jugular vein in doses of 0.02 g., diluted in 10 to 20 ml. of hypertonic glucose or normal saline. The injection, which may be repeated up to 4 times in 24 hours, was given very slowly (1 to 2 minutes) and the dose was reduced to 0.01 g. in two of the smaller infants and increased to 0.025 g. in the child aged 3. Other treatment was also given (subcutaneous infusions, diet, chemotherapy). There were no toxic manifestations due to the drug.

In cases responding favourably there was almost immediate improvement of the toxaemic state. In 11 cases the result was a sudden "resuscitation" within 10 to 15 minutes. In 5 cases the result was good but not quite so dramatic, some evidence of toxaemia persisting. In 2 cases the condition hardly changed. The beneficial result was permanent in 10 cases. It lasted for a few days in 2 cases and only for a few hours in the remaining 6 cases. The final results were: 12 recoveries, 3 deaths among the intestinal group, and 3 deaths among the parenteral group. The author discusses the literature on the mechanism of the toxaemic syndrome,

stressing particularly neuro-vegetative and possibly endocrine factors, the action of histamine or histamine-like substances, and the consequent metabolic derangement. Procaine *in vivo* is split into diethylaminoethanol and *p*-aminobenzoic acid, which is probably the active constituent. Procaine presumably acts as an antihistamine drug and as an antagonist to acetylcholine (thus depressing the parasympathetic.) *P. E. Polani*

1903. **Effect of Influenza Virus Vaccination in Infants and Children, with Antibody Studies.**

By P. COHEN and H. SCHNECK. *J. Pediat.*, **32**, 161–169, Feb. 1948. 20 refs.

In this study the authors continue their previous investigation of the influenza antibody levels in the blood of children (Abstract 1904), and describe the use in 100 children of a vaccine of influenza viruses A and B adsorbed on calcium phosphate. The same technique of titration was used (erythrocyte agglutination-inhibition) and the sera taken before and after inoculation were tested at the same time, because of the variability from day to day of the titre strengths obtained by this method. The inoculations were performed on 100 children aged from 1 month to 18 years over a period of 6 months (October 1946 to March 1947) when an influenza epidemic was anticipated. Only 22 children received a second injection. Local and general reactions to inoculation were slight. The antibody levels were determined before inoculation, and after it at times varying from 6 days to 4 months. The titre rose significantly in the majority of cases over the whole group, the rise being greater in the children over 7 years. The following details illustrate this general statement. The titre-level of 64 is taken as that of " probable immunity " against influenza: before vaccination this immunity level was not reached in any children under 13 years, as regards either the A or the B virus strain; after vaccination, and in the case of the A virus (PR8), the level of 64 was reached in 5 out of the 18 children under 7 years, and in 17 out of the 22 over 7 years. In the case of the B virus (Lee strain), after inoculation the immunity level was reached in 2 out of the 18 under 7, and in 5 out of 22 children over 7 years old. An unequal rise in antibody levels against the two components of the vaccine was shown in some children; the effect of a second injection was studied, but in 5 cases there was no significant change. The authors are continuing their observations on this point, particularly in younger children whose natural supply of antibody is small.

The expected epidemic of influenza did not arrive. During the period of study there were 3 cases of influenza in the 100 inoculated children, and 19 cases in 200 control children. " Although the percentage of cases in the latter is over threefold that of the inoculated children, we feel that the significance of this is far from established in view of the absence of the study during a widespread epidemic involving a larger group of cases. Although our vaccinated group had a reduction in the attack rate, further studies are needed to prove conclusively the clinical efficiency of influenza vaccination in children, and no final conclusion regarding the protective effect of influenza vaccination in children can be drawn from this study ". *C. McNeil*

1904. **Natural Incidence of Influenza Antibodies in Children of Different Age Groups.**

By P. COHEN and H. SCHNECK. *J. Pediat.*, **32**, 154–160, Feb. 1948. 9 refs.

The authors have tried to ascertain the susceptibility of children to influenza by determining the levels in the blood of antibodies against influenza viruses at various ages in childhood. This was done in 13 newborn infants, in 9 infants aged from 1 to 16 months, and in 36 children from 2 to 7 years old. It is admitted that the numbers are small, but it is considered that the consistency of the results and their agreement with those reported elsewhere are significant. The sera were tested against two influenza viruses, the PR8 strain of A, and the Lee strain of B; it was found that the antibody titres at all ages were higher against the A virus than against B. In the case of the newborn infants, the titres were measured in the mothers' sera at the same time; the antibody levels were almost the same in mother and baby in every case, whether the titre was high or low. This result clearly indicated a passive transfer of immunity from the mother, and not an active immunity. This absence of an active and therefore lasting immunity against influenza in infants was shown by the great fall in the antibody levels in the next group of 9 infants (aged 1 to 16 months), the levels in every case being well below the protective minimum. In the third group, the titres remained low at the lower ages, but rose substantially after 5 years of age. This rise is explained by the development of active immunity after infection.

The authors' interpretation of these results is that infants and young children have no natural immunity against influenza (apart from a passive and very fleeting immunity at birth), and that they remain highly susceptible until immunity is developed as the result of clinical infection. They suggest that this susceptibility of young children to influenza might be controlled by prophylactic inoculation of influenza vaccine. *C. McNeil*

1905. **Penicillin in Drops for Prophylaxis Against Ophthalmia Neonatorum. An Single Instillation Method.**

By H. C. FRANKLIN. *Sth. med. J.*, **41**, 320–325, Apr. 1948. 3 figs., 4 refs.

The author, at the John Gaston Hospital, Memphis, Tennessee, instilled 4 drops of penicillin (crystalline sodium salt, 2,500 units per ml. of

isotonic sodium chloride) into the eyes of 1,177 infants within an hour of birth, the lids and conjunctiva having been first thoroughly cleansed. He kept the infants under observation in hospital or at home until the seventeenth day. He found that 1.1 per cent developed conjunctival suppuration in hospital, and 2.9 per cent at home. This contrasts with 2.1 per cent when 4 drops were instilled singly over 3 days in an earlier series and with 6 per cent after silver nitrate prophylaxis in another series. The author points out, however, that 4 drops at once is an excessive dose; he also points out that infants in the earlier series were subject to the hazard of other infection, and that the earlier penicillin may have been less effective therapeutically. Of the organisms, two-thirds were staphylococci. There was no instance of gonococcal infection in the two penicillin series with a total of 2,138 cases. *D. Matheson Mackay*

1906. **A Bacteriological Comparison of Penicillin and Silver Nitrate for Prophylaxis Against Ophthalmia Neonatorum.**

By H. C. FRANKLIN. *Mil. Surg.*, **102**, 179–185, Mar. 1948. 3 refs.

The clinical effects of penicillin and silver nitrate used for prophylaxis of ophthalmia neonatorum have already been studied in 1,710 infants over a period of 7 months. This report covers the bacteriological findings in ocular lesions developing after each method of prophylaxis. Cultures were taken from those infants who had a purulent discharge from the eyes while in hospital, and also, when possible from those with purulent discharge at home during the first 2 weeks of life. Of the hospital patients 2.1 per cent had a purulent discharge after penicillin prophylaxis, and 80 per cent of the cultures were positive. Of the children examined at home 3.1 per cent had a discharge after penicillin prophylaxis, 93.3 per cent of the cultures being positive. After silver nitrate prophylaxis, 6 per cent of the hospital patients had purulent discharge with 37.8 per cent of positive cultures. Of the infants at home 2.4 per cent had a discharge, and 100 per cent of the cultures were positive. The gonococcus was found once after silver-nitrate prophylaxis, but never after penicillin prophylaxis. *Falkland L. Cary*

1907. **Aetiology, Clinical Features, Therapy and Prophylaxis of Infective and Septic Conditions in the Newborn Infant.** [In Russian.]

By I. A. STERN. *Akush. Ginek.*, No. 3, 27–32, May–June 1948.

1908. **Further Observations on the Significance of the Blood Pyruvic Acid Level in Infancy.**

By E. C. ALLIBONE. *Arch. Dis. Childh.*, **23**, 7–16, Mar. 1948. 9 figs., 23 refs.

The complete metabolic breakdown of glucose into carbon dioxide and water follows a sequence of stages which have been identified, in man, as far as pyruvic acid; beyond that point the steps are not known, but they would appear to involve inorganic phosphate, metallic ions, manganese, magnesium and cobalt, protein, and one or more of the factors of the vitamin-B complex. An accumulation of pyruvic acid in the blood occurs in a variety of clinical conditions and might be caused either by retardation of its breakdown or by failure of re-synthesis to glucose. The author, who had previously shown that a raised level of pyruvic acid in the blood was to be expected in toxic and infective states even when thiamine intake was adequate, has now extended his investigations to: (1) the effect of giving massive doses of thiamine, both orally and parenterally, and (2) the fall in blood pyruvic acid which usually results when blood transfusions are given to infants suffering from haemolytic anaemia. After discussing his own findings and the reports and theories of other workers, he comes to the conclusion that the rise in blood pyruvic acid in toxaemic and haemolytic states during infancy is not associated with a deficiency of thiamine and is probably unrelated to any of the known factors in the vitamin-B complex. *N. B. Capon*

1909. **The Serum Cholesterol Level of the Prematurely Born Infant and its Mother.**

By M. J. WHITELAW. *J. clin. Invest.*, **27**, 260–262, Mar. 1948. 27 refs.

The serum cholesterol values of the immature infant are the same as those of the full-term infants. The absolute levels and partition of serum cholesterol do not vary with degree of prematurity. The cholesterol levels of mother and infant bear no relationship to each other. The free and ester fraction of cholesterol are found to be approximately 30 per cent and 70 per cent, respectively, in both the foetal and maternal serum. It is suggested that the low cholesterol value obtained in the serum of the prematurely born infant and term newborn may be due to the depressant action of oestrogenic hormones—[Author's summary.]

1910. **Reliability of the Exclusion of Paternity after the MN and ABO Systems as Elucidated by 20,000 Mother–Child Examinations and its Significance to the Medicolegal Conclusion.** [In English.]

By P. H. ANDRESEN. *Acta path. microbiol. scand.*, **24**, 545–553, 1947. 2 refs.

The blood groups of 20,000 mothers and their children have been determined during tests for exclusion of paternity at the University Institute of Forensic Medicine, Copenhagen. In none was any exception to accepted genetic rules demonstrated. The possible errors due to a non-demonstrated N_2 or weak A factor are discussed. The general conclusion as quoted from the "Guidance in Judging of Blood-Typing Results" issued by the Institute is: "Blood typing belongs to the biological methods of examination . . . it may never attain

to absolute certainty. On the whole, however blood typing may be characterized as one of the most reliable biological methods employed in forensic medicine ". *John F. Loutit*

1911. **Physiologic Icterus of the Newborn.**

By A. LOEWY and L. W. FREEMAN. *Amer. J. Physiol.*, **152**, 205–209, Jan. 1948. 1 fig., 17 refs.

The serum bilirubin content of blood aspirated from the umbilical cord of normal infants at normal deliveries and of blood withdrawn from the external jugular vein on the fifth day of extrauterine life has been determined by Evelyn's method (*J. biol. Chem.*, 1937, **119**, 481) in infants fed on breast milk, or a milk of standard formula containing: (1) 3.6 per cent fat; (2) 1.8 per cent fat; (3) 0.03 per cent fat; (4) 5.5 per cent fat. Fifty-one samples of cord blood had an average bilirubin content of 1.33 mg. per 100 ml. (range 0.13 to 5.22); after 5 days 10 infants in group (1) had an average of 5.41 mg. (range 0.366 to 13.114); 12 subjects in group (2) averaged 4.212 mg. (range 0.436 to 8.946); 9 subjects in group (3) averaged 3,093 mg. (range 0.825 to 9.552); 10 subjects in group (4) averaged 3.175 mg. bilirubin per 100 ml. (range 0.325 to 14.4). Of group (4) it is stated " that the diet was inadequately consumed and the figures cannot be considered representative of the true status on this diet ". It is suggested that approximately 50 per cent of the hyperbilirubinaemia of the newborn can be explained on the basis of haemolysis resulting from the ingestion of fat. *C. C. N. Vass*

1912. **Physiological Jaundice of the Newborn. Some New Measurement of the Factors Concerned.**

By P. L. MOLLISON. *Lancet*, **1**, 513–515, April 3, 1948. 1 fig., 24 refs.

The author summarizes previous work which supports the theory that jaundice in the newborn is due to a functional immaturity of the liver. The excess of bilirubin formed in the first few days of life could be excreted by a liver of mature function and jaundice would not appear.

The extent of postnatal haemolysis was studied. Blood from the placenta of a newborn infant was transfused into a second newborn infant, and the survival of the transfused erythrocytes estimated by the differential agglutination method of Ashby. As a control, erythrocytes from adults were transfused to other infants or occasionally to the same infant, and their survival was estimated. From observations extending to 80 or 90 days it was shown that the rate of breakdown of a newborn infant's own erythrocytes during the first 10 days of life is about twice that of the erythrocytes obtained from adults. When allowance is made for the relatively high mean corpuscular volume in the infant, it may be concluded that the production of bilirubin during the first 10 days is 3 times as great as in the adult. Nevertheless, this is not an amount which would produce in the adult the high serum bilirubin levels which are encountered in the newborn. It is suggested that the acceleration rate of red cell destruction in the infant during the first 10 days is due to the less homogenous population of erythrocytes. The bulk of the erythrocytes have a survival time not much shorter than that of the erythrocytes obtained from an adult. The author also found that the rate of removal of bromsulphalein from the plasma of the newborn infant is strikingly lower than the rate observed in healthy adults.

Because the estimation may be affected by different rates of growth in different infants, the author is carrying out further experiments in which placental erythrocytes and adult erythrocytes are transfused to the same infant and their survivals are studied simultaneously. *J. B. Hannah*

1913. **Congenital Hemolytic Jaundice. The Pathogenesis of the " Hemolytic Crisis ".**

By P. A. OWREN. *Blood*, **3**, 231–248, Mar. 1948. 16 figs., 21 refs.

Six cases showing all the criteria of congenital haemolytic jaundice were studied during crises. Jaundice decreased as the anaemia increased; the size of the spleen was unchanged. Severe anaemia developed, with granulocytopenia and thrombocytopenia, the reticulocytes disappeared, serum colour became normal, and the urobilinuria decreased. The marrow now showed aplasia of the red cell precursors. On about the ninth day of the crisis the pro-erythroblasts in the marrow began to regenerate, followed by increased erythropoesis until, on about the fourteenth day, the marrow was crowded with normoblasts and there was a marked reticulocytosis in the peripheral blood. A leucocytosis and increase in the platelets followed, with recovery from the anaemia. It is suggested that the anaemic crises are due to an acute aplasia of the marrow which, with the short life-span of the abnormal red cells present, produces the rapid anaemia. *Marjorie Le Vay*

1914. **Congenital Haemolytic Anaemia and the Rh Factor.** (La malattia emolitica congenita ed il fattore Rh.)

By R. GIUNTINI and G. PASQUINUCCI. *Riv. Clin. pediat.*, **45**, 746–763, Dec. 1947. Bibliography.

From the Paediatric Department of Florence University, the authors report 18 cases of congenital haemolytic disease, and comment on various features. The first case was studied in retrospect, since it occurred when no anti-Rh serum was available. The family history was typical of congenital haemolytic disease. The patient, born in 1938, had a history of kernicterus and residual signs of neurological damage. When the mother was tested in 1946 there was no incompatibility between her serum and the red cells of various donors and of her husband and children. She was given repeated injections of blood from her husband

and the affected child with production of anti-Rh agglutinins. Later the mother proved to be Rh-negative, while all the other members of this family were Rh-positive. Cases 2 to 5 do not present any exceptional features. .The authors comment on the persistence of agglutinins in high titre in the maternal blood after delivery. In cases 6 and 7 blocking antibodies were found in the mothers' blood and the babies were extremely ill. The authors find no correlation between the type of disease (icterus gravis or severe anaemia) and the type of antibody (complete or incomplete) present. The mother was Rh-positive in 7 of the 18 cases of congenital haemolytic disease here studied, a much higher proportion than the usual 5 to 10 per cent.

In cases 13 and 14 the mother was group O Rh-positive and father and children were group A Rh-positive. There was a high maternal titre of anti-A and anti-B agglutinins, a finding to which the authors feel that aetiological significance should not be attached. In most of the cases in which the mother was Rh-positive, the authors consider the possibility of sensitization to subgroups of the Rh-group, not detectable by routine testing with anti-Rh_0 (anti-D) serum.

Family 17 is very interesting. The second pregnancy resulted in the birth of twins, one of whom developed icterus gravis and kernicterus, while the other remained well. Mother, father, and both twins were group A Rh-positive. In family 18 the mother was group A Rh-positive, and the child, with a history and signs of kernicterus, was group O Rh-positive. An attempt was made to produce antibodies in the mother by injections of filial blood, but without any success. This, according to the authors, excludes blood incompatibility and sensitization between mother and child.

The treatment employed by the authors consisted mostly in blood transfusions, repeated whereever necessary. The blood was given in amounts of 80 to 100 ml. or less at a time, and 7 babies were treated in this way. The blood employed was Rh-negative but on occasions Rh-positive blood had to be given without any apparent ill effects. The results of treatment were good.

P. E. Polani

1915. **Hematologic Studies on Children of Rh-Negative Women Compared to those of Rh-Positive Women.**

By E. L. Potter and H. E. Bernstein. *J. Pediat.*, **32**, 246–250, Mar. 1948.

It has been suggested that mild degrees of anaemia in infants may be due to Rh or A-B incompatibility. The authors have investigated 244 apparently normal infants from this point of view, and have studied haemoglobin values, and erythrocyte, leucocyte, and differential counts on the first and eighth days of life. When the results were classified according to the compatibility of the A-B and Rh factors of the mother and child, no haematological differences were demonstrable between those in which the infant's blood was compatible with that of the mother and those in which it was incompatible. Both groups were combined to give normal mean values.

Doreen Daley

1916. **Studies on the Conglutination Test in Erythroblastosis Fetalis.**

By A. S. Wiener and E. B. Gordon. *J. Lab. clin. Med.*, **33**, 181–188, Feb. 1948. 18 refs.

Live sera from sensitized Rh-negative women were studied to discover which of 5 techniques was most sensitive and satisfactory. The blocking test was least sensitive, being negative in 2 out of 7 samples which did not contain complete (agglutinating) antibody; the plasma conglutinin and antiglobulin (the indirect Coombs test) methods were 7 to 20 times more sensitive, and positive in all 9 sera. The albumin-plasma method was most sensitive, being about 30 times more sensitive than the blocking test.

To discover the best methods of demonstrating sensitization of the infant's red cells in cord blood, a study was made of Rh-positive infants born to 11 Rh-negative women with incomplete Rh antibodies (titre 1 to 1,400 by albumin-plasma technique), to 8 women with complete antibodies (titres 1 to 42), to 4 unsensitized Rh-negative women, and of 3 Rh-negative infants born to sensitized Rh-negative mothers. If incomplete antibodies are present, the cells of cord blood are usually coated with antibody so that they are not agglutinated by agglutinating anti-Rh_0 (anti-D) serum, but are agglutinated by adult plasma or albumin-plasma (8 of 11); the direct Coombs test is positive (5 of 5 cases tested); the infant's serum contains antibodies detectable by the albumin-plasma technique (8 to 9), and the icterus index of cord serum exceeds 14 units. If complete antibodies are present in the mother's blood, sensitization of infant's cells is rarer (4 of 8), and in only one case was antibody detected in the cord serum; the icterus index exceeds 12 units. If blocking antibodies are present in mother's serum as a result of sensitization by a previous pregnancy or transfusion, and the infant is Rh-negative, then the cord serum has a titre identical with that of maternal serum; but if complete antibody is present in maternal serum it does not appear in cord serum. In these, and other unaffected infants, the icterus index does not exceed 14 units.

It is concluded that incomplete antibodies readily pass across the placental barrier, but that complete (agglutinating) antibodies do not, unless there is a defect in the placental barrier or breakdown during labour. The occasional failure of the albumin-plasma technique to demonstrate coating with incomplete antibody of infants' Rh-positive cells is explained by the hypothesis that infant's plasma may contain a conglutinoid, which is absorbed by sensitized cells, but fails to agglutinate

them, though preventing the action of adult conglutinin added later; the difference between conglutinin and conglutinoid is analogous to that between complete and incomplete antibody, or complement and complementoid. When maternal serum contains blocking antibodies, the severity of the disease in erythroblastotic infants is roughly proportional to the titre of the antibody.

G. Discombe

1917. **How Important is Transfusion as a Cause of Haemolytic Disease of the Newborn?**

By G. DISCOMBE and H. O. HUGHES. *Brit. med. J.*, **2**, 329–330, Aug. 14, 1948. 12 refs.

1918. **Erythroblastosis Foetalis and the Rh Factor.** (Die foetale Erythroblastose und der Rh-Faktor.)

By A. GYONGYOSSY. *Gynaecologia, Basel*, **126**, 21–32, July, 1948. 2 figs., 6 refs.

1919. **Therapy of Severe Erythroblastosis Fetalis with Repeated and Massive Exchange Transfusions.**

By A. S. WIENER, I. B. WEXLER, and A. SHULMAN. *Amer. J. clin. Path.*, **18**, 141–151, Feb., 1948. 25 refs.

The purpose of this paper is to describe a modification in the authors' method of treating erythroblastosis foetalis by exchange transfusion, and to report successful results in 2 difficult cases. After a discussion of the advantages of exchange transfusion over other forms of treatment in preventing the clumping of red cells *in vivo*, which is responsible for the more serious manifestations of erythroblastosis foetalis, the management of the 2 cases is described in detail. If the radial artery is used for the withdrawal of blood and the saphenous vein for the infusion, 1,000 ml. of blood can be given to an infant within 90 minutes, thus attaining an exchange of approximately 98 per cent of the infant's red cells. [For technical details and for information concerning the antenatal blood tests recommended, the original paper should be consulted.] In the 2 cases reported the pregnancies were terminated prematurely by Caesarean section. In the first case an exchange transfusion of 500 ml. of blood was given but, since progressive manifestations of the disease continued, the exchange transfusion was repeated on the following day, when the disease was arrested and recovery followed. In the second case, in an infant weighing only 4½ lb. (2 kg.), 1,000 ml. of blood were infused and 950 ml. removed. Jaundice developed but cleared within a fortnight, and no signs of toxicity were seen.

L. J. Davis

1920. **Exsanguinating Transfusion in the Treatment of Erythroblastosis Foetalis.** (Exsanguinační transfuse pri léčení fetální erythroblastosy.)

By K. RASKA and A. BERNARD. *Cas. Lék. ces.*, **86**, 1517–1521, Dec. 22, 1947. 4 refs.

Three cases of erythroblastosis foetalis were successfully treated by exsanguinating transfusion. The Rh-positive blood of the patients was withdrawn from the radial artery and replaced by Rh-negative donor blood through the saphenous vein or the cubital vein with a 10-ml. syringe. Neither citrate nor heparin was added. Some 380 to 430 ml. of Rh-positive blood was withdrawn and 450 to 590 ml. of Rh-negative blood transfused. In one baby the treatment was repeated within 48 hours of birth. Here, 470 ml. Rh-positive blood was withdrawn and 880 ml. of Rh-negative blood given. The Rh-negative blood cells survived for 75 to 80 days. Breast-feeding was started when the Rh antibodies had disappeared from the breast milk (12 to 14 days after birth). No sequelae were observed. The indication for this treatment is the presence of clinical signs of the disease in the newborn, or of Rh antibodies in its serum or in the cord blood. During pregnancy repeated serological controls in suspected cases will facilitate early diagnosis. Where a high or rising antibody titre is found the induction of labour 2 to 3 weeks before term is advised.

M. Dynski-Klein

1921. **The Economics of Infant and Child Nutrition.**

By N. B. TALBOT, W. W. PICK, and S. L. WELLS. *New Engl. J. Med.*, **239**, 79–82, July 15, 1948. 14 refs.

1922. **Formula Rooms For Newborn Infants in Lying-in Hospitals. A Preliminary Study on Supervision and Certain Technics for Preparation.**

By H. M. WALLACE, H. ABRAMSON, and M. A. LOSTY. *Pediatrics*, **1**, 758–766, June, 1948. 21 refs.

1923. **Some Observations on the Feeding of Premature Infants Based on Twenty Years' Experience at the New Haven Hospital.**

By G. F. POWERS. *Pediatrics*, **1**, 145–158, Feb., 1948. 4 figs., 27 refs.

The author discusses various infant dietaries, and points out how his studies of them 20 years ago led him to use as a routine for all infants not breast-fed an artificial feed relatively high in protein, carbohydrate, and minerals, and low in fat. This was obtained by using a mixture of whole and skimmed dried milks in the proportion of 7 to 5 with 10 per cent "dextrimaltose" added, giving the following percentage distribution of calories—protein 16 per cent, carbohydrate 66 per cent, and fat 18 per cent.

Premature infants also received this artificial formula when breast milk was not available and were found to thrive better, as judged by growth and freedom from digestive disturbances, than those on human milk. The rate of gain in weight was studied during the third week of life in 41 infants weighing under 2,250 g. Only infants receiving less than 120 calories per kilo body weight per day were included. Comparison of the 24 infants weighing 1,800 to 2,199 g. at birth showed that those on human milk gained an average of 8.4 g. per kilo per day, while those on the half-

skimmed milk gained on an average 11.9 g. per kilo per day, this difference being statistically significant. Thus human milk, which is satisfactory for the full-term infant, is not necessarily the ideal for the premature infant during the first few weeks of life. Reinforcement of breast milk with some form of protein may render it more suitable, and references are made to recent work in this field. Emphasis is laid on the poor absorption of fat in premature infants, whether fed on human or cow's milk, with consequent loss of calories in the stools when the diet is high in fat. A plea is put forward that the analysis of infants' diets should be expressed as a percentage of total calories obtained from protein, fat, and carbohydrate, this being a more intelligible method, as the analysis is in terms of the unit of metabolism—the calorie.

The mortality rates for the past 23 years are cited; no striking change has occurred, nor have any important changes in any of the age groups been noted during the last 13 years. The survival rates for premature infants fed on a half-skimmed milk mixture are as favourable as those reported from other clinics. However, qualitative differences in foods are unlikely to be reflected in the mortality rates for infants during the first days or possibly weeks of life. *P. Poyner-Wall*

1924. **Foetal Mortality in Labour** (Zur kindlichen Mortalitat sub partu.)

By U. VON RUTTE. *Gynaecologia, Basel*, **125**, 29–36, Jan.–Feb., 1948. 5 figs.

In this statistical review of 45,465 births at the Women's Clinic of the University of Basle the average combined stillbirth and neonatal death rate (10 days after delivery) was 3.4 per cent, varying between figures of 5.5 per cent for 1926 and 1.8 per cent for 1924. When the average figures for any 3 successive years are taken there is a 40 per cent improvement for the years 1941, 1942, and 1943 over the average for the first 3 years under review. The decrease in rates for intrauterine death and neonatal death is not so marked as the decrease in the rate for deaths occurring during actual delivery from 1.6 to 0.7 per cent. This is attributed to earlier and more frequent resort to Caesarean section for foetal indications and improvement in technique of breech delivery. Mortality for breech delivery dropped from 6.5 to 2.7 per cent, mortality for forceps deliveries from 10 to 1.4 per cent. The incidence of Caesarean section has risen from 1.2 to 3.6 per cent, and the infant mortality has dropped from 16 to 3.4 per cent. *Elliot E. Philipp*

1925. **Stillbirth from the Obstetric and Legal Standpoints.** (El nacido muerto desde el punto de vista obstetrico y legal.)

By J. M. MONCANUT. *Toko-ginec. pract.*, **7**, 305–328, June, 1948. 6 refs.

MATERNAL MORBIDITY AND MORTALITY.

1926. **Some Considerations on the Classification of Disease after Confinement.** [In Russian.]

By L. I. BUBLICHENKO. *Akush. Ginek.*, No. 3, 25–27, May–June, 1948.

1927. **The Use of the Recovery Room in Lowering Maternal Mortality.**

By L. F. MCLEAN, H. C. MCDOWELL, and M. G. SADUGOR. *N.Y. St. J. Med.*, **48**, 1368–1370, June 15, 1948.

OBSTETRIC OPERATIONS.

1928. **Amniotic Puncture and Amniography.** (La ponction de l'amnios et l'amniographie.)

By L. PORTES and A. GRANJON. *Gynéc. et Obstét.*, **47**, 42–48, 1948. 4 figs., 3 refs.

The authors consider that abdominal amniotic puncture is a safe obstetrical procedure, too little known in France. They use a spinal puncture needle with an attached Claude manometer. In cases of acute hydramnios accompanying monovular twin pregnancy they repeatedly remove amniotic fluid in this way. In cases of retention of a dead foetus they inject 300 to 600 ml. of "serum" [the composition of which is not specified] in order to induce labour. These authors have also injected "serum" as a means of inducing therapeutic abortion by causing intra-ovular hypertension, but with less success. They have used amniography, after injection of aqueous iodide solutions (20 to 40 per cent) diluted in serum, to study the effects of oxytocics in cases of death of the foetus, to locate the placenta, and to diagnose foetal abnormalities. Since the injected fluid is excreted, pyelocystography may also be carried out. *H. Godar*

1929. **The Present Technique of Lower-Segment Caesarean Section in Potentially Infected Cases at the Obstetric Clinic, Lyons.** (La technique actuelle de la césarienne basse dans les cas impurs à la clinique obstétricale de Lyon.)

By P. TRILLAT, R. BURTHIAULT, and —. CHARVET. *Rev. franç. Gynéc.*, **43**, 249–252, June 1948.

1930. **A Technique to Reduce Blood Loss during Cesarean Section.**

By F. M. DULA. *North Carolina med. J.*, **9**, 291–292, June, 1948.

1931. **A Statistical Review of Two Hundred and Forty-one Consecutive Cesarean Sections.**

By T. W. ADAMS. *West. J. Surg. Obstet. Gynec.*, **56**, 243–249, Apr., 1948.

1932. **A Rare Indication for Cesarean Section: Thrombotic Varicosities in the Vagina.** [In English.]

By K. SOIVA. *Acta obstet. gynec. scand.*, **28**, 77–85, 1948. 27 refs.

1933. **Extraperitoneal Cesarean Section for the Infected Case with a Review of Cesarean Deaths in Jefferson County over a 16-year Period, 1931–1946.**

By B. WORD. *J. med. Ass. Alabama*, **17**, 193–301, Mar., 1948. 9 figs., 35 refs.

1934. **The Use of Local Anesthesia in Cesarean Section.**

By J. F. MOHAN. *Cincinnati J. Med.*, **29**, 335–337, June, 1948.

1935. **The Technique of Craniotomy with the High Lying Head.** [In Russian.]

By N. A. TSAVYANOV. *Akush. Ginek.*, No. 3, 21–24, May–June 1948.

MISCELLANEOUS.

1936. **The Conditioning of the Human Fetus in Utero.**

By D. K. SPELT. *J. exp. Psychol.*, **38**, 338–346, June, 1948. 2 figs., 16 refs.

1937. **The Obstetrician and Gynaecologist as a Witness in the Courts.**

By A. L. MCILROY. *Med.-leg. J.*, **16**, 58–66, 1948.

GYNAECOLOGY.

General.

1938. **Behaviour of the Skin Capillaries in Stilboestrol Therapy.** (Sul comportamento dei capillari cutanei durante la terapia stilbenica.) (Ricerche capillaroscopiche.)

By G. MONTANARI and G. SPADEA. *Ann. ital. Chir.*, **24**, 591–599, Nov.–Dec., 1947. 3 figs., 9 refs.

The nail folds of the fingers of 10 patients taking stilboestrol were examined with a capillaroscope. Seven of these patients had carcinoma of the breast, 1 had carcinoma of the uterus, and 2 had Buerger's disease. The capillary loops were increased in number per field, and appeared to be lengthened and widened, and of deeper colour. These changes were more marked in the women than in the 2 men. The changes occurred quite soon after the start of treatment; they reached a maximum in about 12 days and regressed after cessation of treatment. *Tom Rowntree*

Disorders of Function.

1939. **General Concept and Nomenclature of Menstrual Disturbances.** (Concepto general y nomenclatura de las alteraciones de la menstruacion.)

By M. USANDIZAGA. *Toko-ginec. pract.*, **7**, 263–303, June, 1948. Bibliography.

1940. **Investigations on the Origin of Hypomenorrhoea.** (Untersuchungen über die Entstehung der Hypomenorrhoe.)

By F. HOFFMANN. *Zbl. Gynäk.*, **69**, 1052–1057. 1947. 3 figs., 5 refs.

Twenty-three patients whose genital organs appeared normal on clinical examination but whose menstrual periods, occurring at intervals of from 26 to 30 days, lasted for not longer than 24 hours and were scanty, were investigated at the Gynaecological Clinic of Berlin University and the Huyssens Memorial Hospital, Essen. One patient with tuberculous endometritis was excluded; in 2 women endometrial biopsy was performed a few days after cessation of the period, and in the remaining 20 patients 35 endometrial biopsies were carried out, partly at the end of the proliferative phase, partly at the end of the secretory phase before the period started, and also in the first few days after menstruation.

The histological picture before the period was normal in all cases, in both the proliferative and the secretory phases. Biopsy, performed 1 to 2 days after cessation of the short and scanty menstrual period, showed that only a thin superficial layer of the endometrium had been shed and that the remaining, rather high, mucous membrane was still in the secretory phase; frequently glycogen was demonstrable by Best's method in the glandular cells and lumina. Between the third and fifth days of the cycle, rapid regression of the endometrium took place, with diminution of the oedema of the stroma and narrowing of the glandular lumina, and gradual transition to the proliferative phase. Abnormally slow fall of the progesterone level may be responsible for this atypical variety of menstruation. *N. Alders*

1941. **Causes of Functional Amenorrhoea.** (Uber die Ursachen der funktionellen Amenorrhoe.)

By F. V. MIKULICZ-RADECKI. *Zbl. Gynäk.*, **69**, 1046–1052, 1947.

Because of the recent increase of cases of functional amenorrhoea, the author has studied the cases of 96 women (private patients in Bonn) with amenorrhoea, 55 of whom were not pregnant. He concludes that functional amenorrhoea has recently occurred in Germany not only in patients with labile menstrual cycles, infantilism, or a preclimacteric state, but also in hitherto perfectly healthy women. The reason for this is prolonged physical and mental exhaustion, during which function of the genital organs is suspended, frequently only after exhaustion has been present for a considerable time. The immediate cause of the amenorrhoea is ovarian insufficiency; either the Graafian follicle fails to rupture, through lack of corpus luteum hormone (the size of the uterus remaining normal), or the follicle fails to mature, through lack of follicular hormone as well (the uterus, being hypoplastic). While sudden fright or fear of pregnancy may occasionally be responsible for functional amenorrhoea, there has been physical exhaustion of some duration. *N. Alders*

1942. **Presacral Neurectomy for Dysmenorrhea.** By F. M. INGERSOLL and J. V. MEIGS. *New Engl. J. Med.*, **238**, 357–360, March 11, 1948. 10 refs.

This paper is an analysis of the results of presacral neurectomy in 111 cases of dysmenorrhoea. Other procedures, such as dilatation and curettage or suspension operations, were usually carried out at the same time. The cases are divided into two classes: (1) essential dysmenorrhoea, with severe spasmodic pains coming on soon after the menarche and without physical signs; and (2) acquired dysmenorrhoea, resulting from a demonstrable pathological process (Table 2). Table 1 gives the results obtained in these 2 classes. A much higher proportion of patients with essential dysmenorrhoea were completely cured, the respective figures being 81 per cent and 52.6 per cent.

TABLE 1
Results of Presacral Neurectomy

Result*	Patients with Essential Dysmenorrhoea	Patients with Acquired Dysmenorrhoea
Complete relief ...	73 (81%)	10 (52.6%)
Partial relief	4 (4.5%)	4 (21%)
Failure	12 (14.5%)	5 (26.4%)
Totals	89	19

* There was no follow up study in 3 cases.

TABLE II
Aetiology in Patients with Acquired Dysmenorrhoea

Cause	No. of Cases
Pelvic inflammation	4
Endometriosis	7
Postpartum dysmenorrhoea	5
Postappendectomy dysmenorrhoea	3
Total	19

There were no deaths in this series, but there were 2 cases of post-operative obstruction of the small intestine requiring laparotomy. In 1 case there was severe haemorrhage during the operation due to damage to the left iliac vein.

The causes of failure of presacral neurectomy are examined in detail. In 12 cases the possible causes were psychoneurosis (3 cases), regeneration of nerves (2 cases), and incomplete sympathectomy (7 cases). The oestrogen test was found useful in eliminating the psychoneurotic group. Ovulation is prevented by administration of oestrogens for 20 days; in normal women a painless withdrawal bleeding occurs 2 to 8 days later, but in some cases even this type of bleeding is painful, revealing a psychoneurotic tendency, which contra-indicates operation. The test was carried out in 35 patients on whom a neurectomy was performed later; 32 had painless anovular bleeding and of these 27 were relieved by the operation; 3 had painful anovular bleeding, and obtained no relief. Regeneration of the nerves is a rare cause of failure. In such a case operation appears to be a success, but after several months or even years the dysmenorrhoea returns. Sympathetic fibres may be missed at operation in 2 places; the branches from the fourth lumbar ganglion may pass deep to the arteries instead of anterior to them; or the large trunk, which in some cases runs near to the inferior mesenteric vessels, may be retracted far laterally if the sigmoid has a free mesentery, and thus escape dissection.

After presacral neurectomy 24 patients had children. Of these, 8 patients had almost complete freedom from pain during the first stage of labour, but dilatation of the perineum caused pain in every case. Presacral neurectomy acts by breaking the referred-pain arc, which consists of the presacral nerve, the cord, and the corresponding sensory nerves. Afferents from the fundus are believed to pass to the eleventh and twelfth dorsal segments, afferents from the cervix to the first lumbar segment. In 7 cases pain was relieved except for low backache; it may be, therefore, that in some cases afferents from the cervix pass to the cord by another route, perhaps with the parasympathetic fibres to the second, third, and fourth sacral segments. This is supported by Meigs's finding that passage of a sound through the cervix is still painful after neurectomy, although endometrial curettage is painless. Tiny areas of endometriosis were found in 11 per cent of the cases of essential dysmenorrhoea (average age 24 years), showing that this condition may start very early in life. In 3 cases acquired dysmenorrhoea dated from appendicectomy. No reason for the pain was found at operation, and it was completely relieved by presacral neurectomy. *Margaret Puxon*

1943. **On Intra-abdominal Haemorrhage Originating from the Female Sex Organs.** (Nói ivarszervi eredetú hasüri vérzések különleges okairól.) By M. ACS. *Orv. Lapja*, **4**, 464–468, Apr. 4, 1948. 4 figs., 9 refs.

1944. **Uterine Haemorrhage.** (Hemorragia uterina disfuncional.) By R. PECORONE. *Rev. méd. Rosario*, **38**, 363–385, June 1948. 6 refs.

1945. **Atypical Menstrual Bleeding in Abnormal Conditions of Life.** (Atypische Regelblutungen bei abnormen Lebensbedingungen der Frau.) B. F. SPACKMANN. *Zbl. Gynäk.*, **69**, 1077–1085, 1947. 4 figs., 14 refs.

Comparison of 46 cases of functional menorrhagia and metrorrhagia necessitating curettage in women

between the ages of 20 and 39, seen at the Gynaecological Clinic of Königsberg University in 1937 and 1938, with 65 similar cases observed during 1942–3, showed an increase in such cases almost entirely among women between the ages of 20 and 29. The curettings of 88 of these patients were examined histologically; in 18 per cent the histological picture was normal. In the remaining cases the following abnormalities were detected: congestion of the proliferating mucous membrane (11 per cent), irregularity of the proliferating endometrium (8 per cent), endometrial hyperplasia (35 per cent), retarded shedding of the mucous membrane (7 per cent), irregular shedding of the endometrium (11 per cent), congestion during the secretory phase, irregularity of the secreting endometrium, and hyperplasia during the secretory phase. The author believes that these abnormalities were due to worry and excessive physical exertion, though a proportion of his patients were " cyclelabile ". Curettage, followed by application of a 5 per cent formalin solution to the uterine mucous membrane generally cured the atypical bleeding.

N. Alders

1946. **Rupture of the Vaginal Vault during Coitus.**
By A. W. DIDDLE. *West. J. Surg. Obstet. Gynec.*, **56**, 414–416, July 1948. 36 refs.

1947. **Vaginal Lacerations due to Coitus.** (Lacerazioni vaginali da coito.)
By T. NOBILE. *Ginecologia, Torino*, **14**, 172–184, Apr. 1948. 18 refs.

1948. **Dyspareunia: A Problem for the General Practitioner.**
By R. T. FRANK. *J. Amer. med. Ass.*, **136**, 361–365, Feb. 7, 1948. 9 refs.

Dyspareunia is a common symptom and responsible for much unhappiness. The family doctor is usually the first to be consulted, but often is ill qualified to give advice. In the hope of providing relevant information for the guidance of practitioners, the author reviewed the case records of 349 private patients who had consulted him because of dyspareunia. This represented 1.5 per cent of the patients he had seen over a selected period; 105 patients (29.6 per cent) complained only of dyspareunia, 165 (47.7 per cent) gave it as their main complaint, and 79 (22.7 per cent) mentioned it incidentally. Although 193 (55.3 per cent) had never conceived, only 39 complained of sterility. In 114 patients the dyspareunia had been present since marriage, and the author believes that the seriousness of dyspareunia is proportional to the length of time it has existed. Local introital causes were abnormalities and lacerations of the hymen and inflammatory lesions, all of which responded to local treatment. In 7 cases a congenital septum required excision. Seventy patients complained of an acquired dyspareunia due to introital causes of which the commonest was stenosis after perineorrhaphies and episiotomies. This stenosis was present in 46 patients, while 23 had menopausal involution.

Deep dyspareunia was due chiefly to retroflexion with associated ovarian prolapse and to pelvic inflammation. The former condition was treated by daily assumption of the knee-chest position and by the insertion of a Hodge pessary. In inflammatory conditions the underlying lesion was treated by chemotherapy, rest, and diathermy. Less common causes of deep dyspareunia were the excessive use of contraceptive diaphragms with resultant trauma to the utero-sacral ligaments, and endometriosis of the pouch of Douglas.

When both introital and deep dyspareunia were complained of the usual cause was inflammation. Sixty-three patients (17.5 per cent) had normal pelves and in 24.6 per cent of the total series the cause was psychogenic. In these the dyspareunia is a defence mechanism, and investigation of 36 husbands revealed such male causes of disharmony as impotence, excessive coitus, premature ejaculation, and lack of sympathy. In these cases the co-operation of the husband should be sought and the handling of the patient herself demands tact and kindliness. At the first interview coitus is forbidden, twin beds are advised, and hot sitz baths and sedatives are prescribed. At the next interview, approximately a week later, the patient is instructed in the insertion of lubricated " pyrex " vaginal tubes of ⅝ in. and 1 in. (1.5 and 2.5 cm.) diameter. When the patient can insert the smaller tube herself she is instructed to do this for 10 minutes twice daily by the clock for 1 week. The larger tube is used in the second week. The results of this treatment have been excellent.

J. Stallworthy

1949. **Hymenovestibulitis localis. A Frequent But Disregarded Cause of Dyspareunia.** [In English.]
By J. G. H. HOLT. *Gynaecologia, Basel*, **126**, 39–42, July 1948. 2 figs.

1950. **An Evaluation of Infertility Factors.**
E. W. OVERSTREET. *Calif. Med.*, **69**, 32–36, July 1948. 15 refs.

1951. **The Sterile Marriage.** (A meddó házasság.)
By B. GYULAI. *Orv. Lapja*, **4**, 425–429, Mar. 28, 1948.

1952. **Neuro-endocrine and Psychodynamic Factors in Sterility.**
By H. B. FRIEDGOOD. *West. J. Surg. Obstet. Gynec.*, **56**, 391–398, July 1948.

1953. **A Survey of 754 Cases of Sterility Treated between 1940 and 1946.**
By W. WEINBERG. *S. Afr. med. J.*, **22**, 5–18, Jan. 10, 1948. 2 figs., 16 refs.

The author considers that sterility exists if a couple have been married for at least 2 years and no contraceptives have been employed for at least

1 year. Cases of absolute sterility, cases of relative sterility (one child born from either the present or a previous marriage), and cases of previous abortion are included.

The male with subnormal semen is referred to the urologist; cases have been treated by androsterone injections over periods of up to 6 months, and other patients have been given dry thyroid. Conception has been noted, however, when the husband's sperm count has not exceeded 10,000,000 per ml.

In the examination of the female, a sound is passed to exclude spasm of the internal os. Where this is encountered, the cervix is dilated to No. 5 Hegar without anaesthesia. Cervical erosions are treated by application of iodized phenol, " negatan ", and 2 per cent aqueous mercurochrome in turn, several times if necessary. Surgical diathermy is not thought to accelerate healing. Coincident trichomonas infections are considered to delay the healing of erosions and are treated by application of 3 per cent hydrogen peroxide and 2 per cent gentian violet, insufflation with an acetarsol powder, and insertion of " floraquine " tablets twice daily. Retroflexion of the uterus is corrected and a Hodge pessary inserted; where correction is not possible Gilliam's operation is performed. Air insufflation is carried out within 1 week of the end of the period, and is repeated twice if the result indicates tubal blockage, spasm, or stenosis. Auscultation of the abdomen and the complaint of shoulder pain are used to assess tubal patency, as well as the manometric readings. Lipiodol hysterosalpingography is performed if 3 air insufflations have given negative results. Where the tubes are not patent short-wave pelvic diathermy is administered twice weekly (except during the week of the period), and air insufflation is repeated twice monthly over a period of 6 months; in many such cases patency was re-established.

Morning oral temperature is recorded over a 2-month period to detect ovulation. Endometrial biopsy is performed on the first day of menstruation. Where repeated biopsy shows that menstruation is anovular, cases have been treated by injections of " synapoidin " (follicle-stimulating and luteinizing hormones) on the fourth, sixth, eighth, tenth, and twelfth days of the cycle. Other cases have been treated by injection of gonadotrophins, or oestrogens and progesterone. The Huhner post-coital test and Miller-Kurzrok lytic test are also carried out. Where there is a history of previous abortion complete abstinence from intercourse and adequate rest are advised during pregnancy. Vitamin E, 50 mg. twice daily and oral progesterone, 10 mg. daily, are given until the ninth month.

Of 754 cases of sterility, 563 were absolute and 191 relative. The average age of the female was 31 years; the average duration of marriage before treatment was 7 years, and the average duration of attempts to bring about conception 6.1 years. There was a history of previous abortion in 150 cases. In 42 cases (5.5 per cent) both male and female partners were found to be at fault. There were 9 subsequent pregnancies (21 per cent). In 63 cases the male was at fault (8.3 per cent). There were only 11 subsequent pregnancies (17 per cent). In 733 cases the female was considered to be at fault (97.2 per cent). The fault was tubal in 445 cases (61 per cent). Treatment resulted in 293 subsequent pregnancies (66 per cent successful). Nine cases of tubal block were treated by salpingostomy, with 3 subsequent pregnancies. There were 97 cases of anovular menstruation (13 per cent), repeated endometrial biopsy showing no evidence of luteinization; 78 cases were treated by endocrine therapy, with 60 subsequent pregnancies (62 per cent successful). In 413 cases (56.3 per cent) the fault was considered to be " uterine ". There were 47 cases of retroflexion of the uterus; 33 were treated by replacement and insertion of a pessary, and 14 by Gilliam's operation; 35 patients became pregnant (75 per cent successful). Ovarian tumours and fibroids were found in 68 cases; 28 cases were treated conservatively and 40 by operation, including 14 by myomectomy. There were 39 pregnancies (57 per cent successful). " Infected cervical mucus " was treated in 54 cases, with 47 subsequent pregnancies (88 per cent successful).

Artificial insemination with the husband's semen was employed in 21 cases. On the average 16 inseminations over a period of 7½ months were made. There were 11 pregnancies, including 2 cases of twin pregnancy (52 per cent successful). In the whole series of 754 cases there were 400 pregnancies (53 per cent successful). Of these 22 ended in abortion (5.5 per cent); there were 3 ectopic pregnancies (0.7 per cent).

[The abstracter finds much to criticize in this article. The author's standard of sterility is not that generally accepted. The author states that retroflexion tends to hinder conception, but later accepts the principle that retroflexion is no hindrance to pregnancy. Nevertheless, he either corrects the position or performs Gilliam's operation in all cases of retroflexion. Much of the treatment appears superfluous. Thus androgen therapy is given to the male with subnormal semen, and a sperm count persistently below 100,000,000 per ml. is considered subnormal. In one case quoted, endocrine therapy was given to induce ovulation after only one negative endometrial biopsy. In cases of habitual abortion vitamin E and progesterone are given until the ninth month of gestation.] *Ian T. Fraser*

1954. **Results of Treatment of Sterility in Women.** (Resultater af Behandling af Sterilitet hos Kvinden.)

By J. HOFFMEYER. *Nord. Med.*, **39**, 1420–1425, July 30, 1948. 3 figs., 14 refs.

1955. **Variations in Spermatogenesis of Oligospermic Men.**

By B. ZONDEK, Y. M. BROMBERG, and Z. POLISHUK. *Nature, Lond.*, **161**, 176, Jan. 31, 1948.

Two women, whose husbands had sperm counts of 5,000,000 and 10,000,000 per ml., became pregnant; this suggests that the low counts were not invariable. Twenty-one men with a low sperm count when first examined (all the counts were under 30,000,000 and 12 were under 10,000,000 per ml.) were re-examined 5 to 7 times, always at least 5 days after ejaculation. In 13 of the subjects there were fairly consistent low counts with variations of less than 12,000,000 per ml. The counts in the other 8 cases fluctuated considerably, 2 specimens from the same man differing by as much as 43,000,000 per ml.; 5 of these men had 60,000,000 sperms per ml. in some ejaculates and 2 of their wives became pregnant. It is concluded that oligospermia may be constant or periodic and that single counts may mislead. *Peter C. Williams*

1956. **Variations in Spermatogenesis of Oligospermic Men.**

By M. H. JACKSON and C. LARVEY. *Nature. Lond.*, **162**, 67, July 10, 1948. 2 refs.

1957. **Semen Analysis in 204 Cases of Sterile Marriage.**

By J. P. ROBERTSON. *Sth. med. J.*, **41**, 537–543, June 1948. 4 refs.

1958. **Frequency of Undescended Testis and its Importance in Sterility.** (Die Häufigkeit des Kryptorchismus und seine Bedeutung für das Sterilitätsproblem.)

By W. BREIPHOL and H. U. BALZER. *Zbl. Gynäk.*, **69**, 1139–1147, 1947. Bibliography.

Undescended testicles were found in 90 out of 4,500 boys examined (2 per cent). The average age of the boys was 12 years. In 58 cases non-descent was unilateral, and in 32 cases bilateral. Follow-up examination at the age of 15 revealed that spontaneous descent had taken place in 46 boys; 25 boys had been treated surgically (orchiopexy); in 10 cases the testicles were still undescended, and 9 boys failed to report for re-examination. In view of these observations and of reports in the literature, it is thought correct to wait until the onset of puberty, that is, until the age of 15, before treating non-descent of testicles. Surgical treatment should be preceded by administration of hormones. Apparently good results of surgery do not imply that the patient possesses full reproductive powers. The latter should be assessed before the patient marries or at an earlier date, so that statistics may be compiled on the extent of permanent damage caused by non-descent of testicles and on the significance of this condition in reproduction.

[No new facts are brought out in this paper which, apart from the statistical material collected in Berlin, is mostly speculative.] *N. Alders*

1959. **Genital Complications of Mumps in the Aetiology of Sterility.** (Sulle localizzazioni genitali della parotite nella eziologia della sterilità coniugale.)

By E. ROBECCHI. *Ginecologia, Torino*, **14**, 202–211, May 1948. 21 refs.

Abnormalities of the Reproductive Organs.

1960. **Familial Male Pseudohermaphroditism and the Effects of Surgical Castration.** (Lo pseudo ermafroditismo maschile famigliare ed effetti su di esso della castrazione chirurgica.)

By A. GIUSTI. *Ann. ital. Chir.* **25**, 23–40, Jan. 1948. 9 refs.

Two sisters at the age of 7, one in 1935 and the other in 1937, were operated on for bilateral inguinal herniae. At operation minute testicles (proved microscopically) were found in each inguinal canal. These were removed, and the patients were followed up. In 1946 they were seen and found to have developed into healthy-looking girls, with poor distribution of hair. The breasts were not developed, and there was very little subcutaneous fat on the abdomen or on the thighs The external genitalia were normally female in every way, but clinical examination revealed neither uterus nor ovaries. The girls were normal psychologically, but seemed uninterested in sexual activity. *Tom Rowntree*

1961. **True Hermaphroditism.**

By W. B. STROME. *Amer. J. Obstet. Gynec.*, **55**, 1060–1064, June 1948. 5 figs., 5 refs.

Infections of the Reproductive Organs.

1962. **Possibilities of Antibiotic Therapy in Pelvic Inflammation in the Female.** (Possibilità terapeutiche degli antibiotici nelle flogosi pelviche femminili.)

By T. NOBILE and V. SVRLJUGA. *Ginecologia, Torino*, **14**, 229–256, June 1948. 22 refs.

1963. **Vaginal Abscess due to Perirenal Abscess.** (Coleçã vaginal proveniente de abcesso peri-renal.)

By A. R. DE OLIVEIRA MOTTA. *Rev. Ginec. Obstet.*, **1**, 355–362, June 1948.

1964. **Atabrine in the Treatment of Trichomonas Vaginitis.**

By F. M. DULA. *North Carolina med. J.*, **9**, 309, June 1948.

1965. **Tuberculosis of the Female Genitalia.** (Contributo della tubercolosi genitale femminile.)

By L. NOBILI. *Riv. ital. Ginec.*, **30**, 283–322, 1947. 1 fig., 26 refs.

A study was made of 70 women with genital tuberculosis surgically treated in the Obstetrical and Gynaecological Clinic of the University of Bologna between 1936 and 1946 and selected from 7,653 gynaecological cases admitted. The clinical diagnosis of genital tuberculosis was made in 117 patients (1.53 per cent).

Genital tuberculosis was more frequent in patients

between 21 and 30 years (38.57 per cent of all cases). Some 44 women (62.85 per cent) were sterile; 23 had had full-term pregnancies and 3 had had miscarriages. In 18.75 per cent the onset of menstruation had been delayed. Menstruation had always been regular in 40 per cent and irregular in 30 per cent; in 30 per cent menstrual disorders began with the onset of salpingitis. Hypermenorrhoea was the disturbance most frequently encountered. It is considered that in the majority of cases of genital tuberculosis the infection is of secondary origin. In 59.57 per cent of patients in this survey old or recent tuberculous lesions were found, usually pulmonary or intestinal. When the infection is confined to the genital organs it is haematogenous; in cases of associated peritoneal tuberculosis the infection is a descending one. The lesion was in the Fallopian tubes in 54 cases, in the ovary in 10, in the uterine body in 4, and in the cervix in 2. The peritoneum was involved in 44 cases. The symptoms were pain, leucorrhoea, and metrorrhagia, with pyrexia in some cases. Symptoms had started in 52.85 per cent a month before the patient was admitted; in the remainder the duration of symptoms varied from 1 month to over a year.

Before operation the patients underwent a long period of careful medical preparation, on which the author lays great stress. Subtotal hysterectomy and bilateral removal of the adnexa was performed in 45 cases, total hysterectomy and bilateral removal of the adnexa in 2 cases. Removal of the adnexa was bilateral in 4 cases and unilateral in 2. The tendency in the Bologna clinic is towards a liberal removal of all tuberculous foci and suspected tissues, but a more conservative attitude is adopted in inactive forms, without extensive adhesions, when the uterus is intact and the patient in good general condition. Exploratory laparotomy is chosen, with removal of the infected organs where possible, in diffuse genito-peritoneal fibro-caseous tuberculosis and in the exudative forms. One patient died after operation. The results were classified as very good in 9 cases and good in 56 cases, the condition being unchanged in 4. Five patients died between 2 and 5 years after operation.

[It is not possible to do justice to this valuable article in a short abstract.] *Rina Saunders*

1966. **Hysterosalpingograms in Genital Tuberculosis in Women.** [In English.]

By V. MADSEN. *Acta radiol., Stockh.*, **28**, 812–823, Nov. 13, 1947. 11 figs., 3 refs.

This is a survey of the radiographic findings in 42 patients, in 20 of whom the diagnosis of genital tuberculosis was confirmed by histological examination. In the other 22 there was no such confirmation, but the clinical evidence was in favour of this diagnosis. The author, though admitting that all salpingographic forms may be encountered in tuberculous salpingitis, claims that there are certain features suggestive of a tuberculous aetiology. His remarks refer only to the chronic forms of salpingitis. The most striking feature is the retention of the opaque medium in tubes which show little or no dilatation, in contrast to the marked dilatation that occurs in, for instance, the gonorrhoeal form of the disease. This feature was seen in 29 out of the 42 cases. In addition, there may be evidence of calcification in the tubes, and the contrasting shadows of this and the opaque medium give rise to a characteristic picture. In 2 cases tuberculous endometritis was suspected, because an irregularity of the uterine wall was associated with lack of filling in the tubes. In one case in which the abdominal ostium was patent the contrast medium that had spilled into the pelvis formed globules, indicating ascites. The presence of calcified glands in the pelvis associated with these findings is also in favour of a tuberculous origin. *L. G. Blair*

1967. **Further Experiences in the Roentgen Diagnosis of Tuberculous Salpingitis.** [In English.]

By W. MAGNUSSON. *Acta radiol., Stockh.*, **28**, 824–832, Nov. 13, 1947. 8 figs., 8 refs.

In a previous communication the author, from a study of 12 cases of tuberculous salpingitis verified histologically, described a radiological picture which he claimed to be diagnostic of a tuberculous aetiology. The picture was characterized by uneven, jagged, and ragged mucosal contours and small lumen defects, the anatomical basis for these changes being the swollen and tightly folded mucous membrane. After a study of 7 fresh cases and re-examination of all cases with tubal occlusion, a second type of salpingographic picture is described, characterized by even, straight, or rigid mucosal contours and a pipe-like appearance of the tube. In these cases histological examination showed the folds of the mucous membrane to be very adherent to each other and the lumen to be more or less obliterated. Both types may be seen in the same case. Fistulae and abscess-like processes leading from the lumen may also be found in both types. In a control series in which there had been either a gonorrhoeal infection or septic infection after abortion, the appearances described above were absent. It is claimed, therefore, that a pre-operative diagnosis of tuberculous salpingitis is possible in most cases of sterility where tuberculosis is the cause.

The author reports no instances of spreading of the tuberculous process, but states that hysterosalpingography is contra-indicated when clinical signs of active inflammation, whether tuberculous or otherwise, are present. *L. G. Blair*

1968. **Diagnosis of Primary Tuberculosis of the Cervix.** (Le diagnostic de la tuberculose primitive du col utérin.)

By P. NORMAND and P. LABIGNETTE. *Presse méd.*, **56**, 95, Feb. 7, 1948. 1 fig.

1969. **A Case of Genital (Utero-tubo-ovarian) Tuberculosis with Particular Involvement of the Endometrium.** (Descrizione di un caso di tubercolosi genitale (utero-tube-ovaie) con alta prevalenza endometriale.)

By C. P. MORANO. *Monit. ostet.-gynec.*, **19**, 103–114, Mar.–Apr. 1948. 4 figs., 52 refs.

1970. **Penicillin–Procaine in Acute Parametritis and Salpingitis.** (Penicilina–novocaína en las anexo parametritis agudas.)

By M. GONZÁLEZ. *Arch. Soc. Ciruj. Hosp.*, **17**, 507–519, Sept. 1947. 3 figs., 11 refs.

In view of the application of the work of Leriche on procaine block to gynaecological conditions by several authors, and also of the use in inflammatory conditions of the eye of a procaine–penicillin mixture, the author had employed this mixture in the treatment of a series of cases of acute infection of the parametrium and uterine appendages. After discussing at length the innervation of the pelvic organs, he describes his technique in detail and the results in 16 cases. The mixture employed consists of 50 ml. of 1 per cent procaine in which 100,000 units of penicillin are dissolved. Two long narrow retractors are passed into the vagina, and the cervix is pulled to one side by an instrument gripping the posterior lip. A 20-ml. syringe with a fine needle not less than 10 cm. in length is used. The needle is introduced parallel to the cervix and must be inserted to a depth of 1 to 2 cm. into the lateral fornix in order to inject the ganglion of Frankenhaüser. The patient should then complain of pain, and 10 ml. of solution is injected. The needle is partly withdrawn and reinserted to reach the more lateral part of the broad ligament, where a further 10 ml. is injected. The usual precaution of aspiration before injection is taken. The procedure is then repeated on the opposite side. Finally 10 ml. is injected into the posterior fornix, care being taken not to insert the needle for more than 2 cm. in order to avoid entering the pouch of Douglas. Gentleness is essential in the procedure. Five patients felt faint, and there was haemorrhage from the site of puncture in 2 cases, in 1 of which vaginal packing was needed.

In 7 patients who were followed up for 6 months an anatomical and functional cure was obtained, though in 2 cases a second injection was necessary. In 6 cases there was either no follow-up study or the period after injection is short, but in most of these the immediate results were satisfactory. In 3 patients the treatment failed; 2 were operated upon for pyosalpinx, and the third had appendicitis. In this latter case, however, the failure of the injection to relieve pain was considered to be a helpful diagnostic feature. After discussing the various theories about the action of procaine, the author puts forward the view that the two drugs have a synergistic action. This treatment is recommended on the grounds that it is successful, economical, harmless, and simple, and can be carried out on ambulant patients. *Bryan Williams*

New Growths of the Reproductive Organs.

1971. **An Experiment With Uterine Cervical Smears in the Diagnosis of Genital Malignancies.**

By G. M. WILCOXON and F. H. FALLS. *Ohio St. med. J.*, **44**, 165–167, Feb. 1948. 7 refs.

Of all primary cancers occurring in women 24.6 per cent arise in the genital tract. Primary breast cancers account for 18.4 per cent. In recent years many workers have shown that malignant uterine neoplasms can be diagnosed by the vaginal smear technique, and that the vaginal smear is also valuable in following the treatment of uterine malignancy by radiation therapy. In the present study the technique of vaginal smear has been applied to the uterine cervix. The method of taking the cervical secretion and the preparation and staining of the slides are described.

Cervical smears were taken from new cases seen at the cancer clinic at Research and Educational Hospitals of the University of Illinois and from patients admitted to the gynaecological wards. Of 236 cases studied, 198 showed no evidence of cancer. In this series of 198 negative cases there were 18 false-positive diagnoses. These are all regarded as mistaken because no positive pathological evidence of malignancy was demonstrated; they represent an error in the total number of cases followed of 7.6 per cent. Of the 236 patients 38 were shown to have cancer. In 2 of these 38 cases the smears were negative: a case of epidermoid carcinoma of the cervix, negative on first smear but positive on a second; and a case of leiomyosarcoma of the uterus from a degenerating fibroid where the neoplasm probably never exfoliated any malignant cells into the uterine canal; the uterine mucosa was normal. The positive cases included 21 of carcinoma of the cervix; in 17 of these there were epidermoid carcinomata and in the rest squamous-celled carcinomata. Seven cases of fundal cancer were seen—4 of adenocarcinomata, 1 of adenocanthoma, and two of leiomyosarcomata. *Lilian Raftery*

1972. **A Correlation between Vaginal Smear and Tissue Diagnosis in 1045 Operated Gynecologic Cases.**

By N. P. ISBELL, J. F. JEWETT, M. S. ALLAN, and A. T. HERTIG. *Amer. J. Obstet. Gynec.*, **54**, 576–583, Oct. 1947. 36 refs.

In 1,045 cases the authors compared the relative values of vaginal smears and of biopsy and curettage in the diagnosis of uterine cancer. They also studied the practical aspects of the technique, with reference to the special training required. The material was collected from in-patients on the day before they underwent operation and from out-patients from whose cervices biopsy specimens were subsequently taken. Smears were prepared and stained by the Papanicolaou technique and interpreted by one or other of the authors who, at

the time of giving his report, was ignorant of the clinical history and biopsy diagnosis. The smear was reported to be positive or negative for carcinoma, and this first report was accepted for the purpose of the study, irrespective of any later diagnosis.

The results were divided into three groups. The first included 1,000 cases in which the diagnosis from the biopsy specimen was definite. The second consisted of 41 in which the diagnosis was doubtful. The third consisted of 4 cases in which carcinoma was encountered elsewhere than in the uterus or vagina. In the first group there were 60 cases of carcinoma—40 of the cervix, 18 of the body, and 2 of the vagina. In 39 cases of carcinoma of the cervix, 15 cases of carcinoma of the corpus uteri, and the 2 cases of vaginal carcinoma, the diagnosis was made from the vaginal smears. In the 60 cases of proven carcinoma there were, therefore, 4 false-negative results from the smear technique. In the remaining 940 cases there were 11 false-positive results from the smears. As would be expected, there was a greater incidence of disagreement between the results of vaginal smear and biopsy in the second group of doubtful cases. Group 3 contained 4 cases of carcinoma—1 of the Fallopian tube, 1 of the bladder, 1 of the urethra, and 1 of the vulva—and in each case the smear revealed malignant cells. The time taken to report on an average smear was from 15 to 20 minutes, while in difficult cases as long as 2 hours was necessary. The authors concluded that vaginal smears offer a valuable accessory aid to diagnosis, but note that in comparison with biopsy the method has an irreducible limit of error.

J. Stallworthy

1973. **Value in Clinical Diagnosis of Study of the Morphological Components in the Vaginal Smear.** (Uber die klinisch-diagnostische Auswertungsmöglichkeit der morphologischen Bestandteile im Vaginal abstrich der Frau.)

By H. PERLI. *Acta obstet. gynec. scand.*, **28**, 38–76, 1948. 51 refs.

1974. **Practical Application of the Vaginal Smear as a Method in Clinical Gynecology.**

By I. SLOVIN, W. B. SILBERBLATT, and H. B. SAFFORD. *Delaware med. J.*, **20**, 109–112, June 1948. 10 figs., 1 ref.

1975. **The Vaginal Smear. Its Value to the Internist, with Report of Diagnosis of Unsuspected Uterine Cancer in Four Cases.**

By M. FREMONT-SMITH and R. M. GRAHAM. *J. Amer. med. Ass.*, **137**, 921–922, July 10, 1948. 11 refs.

1976. **Cytological Diagnosis of Uterine Cancer.** (Citodiagnóstico del cáncer uterino.)

By G. TERZANO. *Rev. mex. Cir. Ginec. Cáncer*, **16**, 11–17, Jan. 1948.

1977. **Prognostic Value of Erythrocyte Sedimentation Rate in Malignant Tumours of the Female Genitalia.** (Sul valore prognostico della velocità di sedimentazione dei tumori maligni dell'apparato genitale femminile.)

By Z. SISINO. *Ginecologia, Torino*, **14**, 185–188, Apr. 1948.

1978. **Leucoplakia of the Vulva. Preliminary Report.**

By N. F. MILLER, M. H. PARROTT, J. STRYKER, G. M. RILEY, and A. C. CURTIS. *Amer. J. Obstet.*, **54**, 543–560, Oct. 1947. 9 figs., 18 refs.

The term leucoplakia is used to include both the hypertrophic and the atrophic phases of the disease more commonly referred to as kraurosis. The records of 153 patients who had attended the University of Michigan Hospital since July, 1931, were studied. Thirty-six cases have been investigated in more detail since January, 1946, but 25 of these were also included in the previous group referred to by the authors as the "pre-study group". There were no Negresses in the series. In this pre-study group the average age was 55.6 years, the eldest patient being 80 and the youngest 23. One patient, aged 23, was pregnant; 114 patients were post-menopausal, and in 10 the menopause had been induced artificially; 33 had an associated carcinoma of the vulva. In 54 cases a vulvectomy was performed, with a recurrence of symptoms in 13.

The group of 36 patients were studied according to an agreed plan, which included investigation of the dermatological, allergic, and psychiatric aspects of each case. Focal sepsis was looked for. Urine and gastric contents were analyzed. Assays of hormones were made, including the oestrogens, follicle-stimulating hormone, and 17-ketosteroids. The lesions were photographed, biopsies, smears, and cultures were studied, and the blood examinations included serological tests and estimations of ascorbic-acid and vitamin-A levels.

In 10 of 24 patients, in whom a complete blood study was carried out, there was evidence of infection as indicated by raised erythrocyte sedimentation rate, toxic granulations, or leucocytosis. No cause-and-effect relation was established between emotional instability and the disease. Chronic irritation of the vulva was not found to be an aetiological factor. Eleven of 25 patients examined for allergy had an allergic background and in 2 some relief was obtained by removal of the allergen. A low vitamin-A level was observed in the plasma of only 1 of 10 patients investigated, but achlorhydria was found in 6 of 12 patients studied. Two of these were suffering from pernicious anaemia. In 14 of 22 patients the ascorbic-acid level in blood was found to be normal or high. In 22 of 26 patients oestrogen levels were normal. No significant features were found in the excretion of 17-ketosteroids or follicle-stimulating hormone.

J. Stallworthy

1979. **An Epidermoid Cyst of the Vulva.** (Una cisti epidermoide della vulva.)

By V. ARNONE. *Monit. ostet.-gynec.*, **19**, 115–125, Mar.–Apr. 1948. 2 figs., 18 refs.

1980. **Bowen's Disease of the Vulva.** (Vulvite erosiva epiteliomatosa (Morbo di Bowen).)

By F. LISI. *Ann. ital. Derm. Sif.*, **3**, 181–189, May–June 1948. 1 fig., 17 refs.

1981. **A Study of Pre-carcinoma of the Vagina.** (Contribución al estudio del epitelioma incipiente de la vagina (Precáncer de vagina).)

By J. VANRELL. *Rev. esp. Obstet. Ginec.*, **7**, 143–147, May–June 1948. 2 figs., 6 refs.

1982. **A Consideration of Some Uterine and Ovarian Tumors.**

By A. H. CURTIS. *West. J. Surg. Obstet. Gynec.*, **56**, 404–406, July 1948. 2 figs.

1983. **Ligation of the Internal Iliac Artery in Haemorrhage due to Uterine Carcinoma.** (Uber die Unterbindung der Arteria hypogastrica bei Blutungen infolge Gebärmutterkrebs.)

By W. MICHEL. *Zbl. Gynäk.*, **69**, 1188–1192, 1947. 3 refs.

1984. **Prognosis and Treatment of Carcinoma of the Body of the Uterus.** (Le pronostic et le traitement du carcinome du corps utérin.)

By R. BOURG and J. FALLY. *Brux-méd.*, **28**, 1481–1493, July 18, 1948. 3 figs., 25 refs.

1985. **Metastases in the Bony Pelvis Due to Carcinoma of the Body of the Uterus.** (Beckenknochenmetastase eines Korpuskarzinoms.)

By V. GRUNBERGER. *Krebsarzt*, **3**, 262–267, July 1948. 1 fig.

1986. **Supraclavicular Metastases from Carcinoma of the Uterus.** (Le metastasi sopraclaveari del cancro dell'utero.)

By F. DE SIMONE. *Radiologia, Roma*, **4**, 109–122, Apr.–June, 1948. 23 refs.

1987. **Phosphorus Metabolism in the Normal and in Pathological Conditions. II. Ribonucleic Acid in Inflammations, Erosions and Cancer of the Human Cervix Uteri.** [In Russian.]

By A. G. ANDRES and K. A. PEREVOSHCHIKOVA. *Arkhiv Patologii*, **10**, 3–11, 1948. 6 figs., 15 refs.

1988. **Surgery in Carcinoma of the Cervix.** (La cirugia en el cancer del cuello uterino.)

By C. ZUCKERMANN. *Rev. mex. Cir. Ginec. Cáncer*, **16**, 3–8, Jan. 1948. 21 refs.

1989. **Dosage Estimation and Distribution in the Radium Treatment of Carcinoma of the Cervix Uteri. A New Method and its Clinical Applications.**

By M. LEDERMAN and L. F. LAMERTON. *Brit. J. Radiol.*, **21**, 11–26, Jan. 1948. 24 figs., 13 refs.

The authors describe fundamental work on dosage in radiotherapy of carcinoma of the cervix as employed at the Royal Cancer Hospital, London. They describe a technique of determining the dose at a point in the pelvis during the radium treatment which can be applied to any individual case. They use a double-shift radiographic method of estimation of the positions of the radium sources, from which they reconstruct actual positions in space. They then use Mayneord's contour-projector to obtain the actual dosage delivered. The method seems simple and reasonably quick. By means of a special "localiser" and opaque media the authors study the dosage received by normal structures and by lymph-nodes. Among their investigations they describe an ingenious adaptation of a Ferguson mouth-gag, by which they have demonstrated a variation in vaginal vault diameter from 4 to 11 cm., and show a diminution between successive radium treatments of 0.5 to 1.5 cm. Their aims are: (1) To estimate the dose received by diseased tissues. (2) To estimate the dose received by the adjacent normal tissues. (3) To investigate the anatomical and technical factors affecting the dose. (4) To help to correlate radium and X-ray treatments. Each of these is discussed in some detail.

[This paper records most interesting progress in the work begun by the abstracter on these problems. It is to be noted that the authors do not discuss the problems of the shape of the volume-dosage delivered, which may not correspond with the volume of the tumour tissue involved. The abstracter has found that dosage estimated at one point only may be misleading (Sandler, *Proc. R. Soc. Med.*, 1945, **38**, 175) because the point may really be a point of maximum dosage for that particular isodose surface, which may rapidly recede from the pelvic wall. Although much more work requires to be done on the actual shapes of volume-dosage obtained and on the particularly difficult problem of matching this shape to the X-ray volume dosage, this paper is nevertheless a notable contribution to a fundamental problem in the treatment of carcinoma.] *B. Sandler*

1990. **Late Results of Radium Therapy for Carcinoma of the Uterine Cervix.**

By H. H. BOWING and R. E. FRICKE. *J. Amer. med. Ass.*, **137**, 935–942, July 10, 1948. 19 refs.

1991. **42.5 Per Cent of Complete Cures in 41 Cases of Carcinoma of the Cervix.** (42.5 Prozent absolute Heilung bei 41 Kollumkarzinomfällen.)

By F. FRIEDL. *Zbl. Gynäk.*, **69**, 1192–1199, 1947. 2 figs., 7 refs.

1992. **Experimental Studies on the Pathogenesis and Histogenesis of Ovarian Tumours in Mice.**

By M. H. LI and W. U. GARDNER. *Cancer Res.*, **7**, 549–566, Sept. 1947. 22 figs., bibliography.

The authors describe a number of granulosa-cell and luteal-cell tumours which arose from intrasplenic transplants of ovarian tissue in castrated male and female mice. Most of the tumours

developed after 7 months from the time of operation. With one exception, no tumours arose from subcutaneous or intratesticular grafts of ovarian tissue in either intact or castrated male or female mice. Ovarian hormones produced by intrasplenic ovarian grafts are inactivated by the liver, and there is concomitant increase in the production of pituitary gonadotrophins in these mice. The endocrine imbalance so established results in sustained excessive stimulation of the ovarian transplants, and this is believed to be responsible for the frequent development of tumours from transplants in the spleen, in sharp contradistinction to those in other situations. Possibly similar gonadotrophic overaction is responsible for the granulosa-cell tumours which arise in irradiated ovaries.

R. A. Willis

1993. **Malignant Tumours of the Ovary.**

By J. B. MONTGOMERY. *Amer. J. Obstet. Gynec.*, **55**, 201–217, Feb. 1948. 6 refs.

In this study the author reviews all the malignant tumours of the ovary treated at the Jefferson Medical College Hospital, Philadelphia, between 1921 and 1946. Altogether 107 are reviewed, 84 of which were primary carcinomata, 7 secondary to uterine cancers, 2 adenocarcinomata occurring in teratomata, 10 granulosa-cell tumours, 1 a Krukenberg tumour, 2 dysgerminomata, and 1 a Brenner tumour. The present paper deals chiefly with the 84 cases of primary cancer. Most of these occurred in patients aged from 40 to 49, but 1 patient was 16 and one 73; 57 per cent were between the ages of 40 and 60, and 31 patients had passed the menopause. Of the married women 11 per cent were sterile.

The chief symptoms were pain (53 cases) and enlargement of the abdomen (59 cases). Nausea and vomiting, loss of weight, backache, weakness, and dyspnoea were mentioned less often; 14 per cent had bleeding and of these about half had associated fibroids. The four factors particularly studied were (*a*) the extent of the growth, or the operability; (*b*) the grade of malignancy; (*c*) the histological type of tumour; (*d*) the influence of X-ray therapy on the lesion. The tumours were classified as either serous or pseudo-mucinous, and divided into three histological grades of malignancy: Grade I or low-grade malignancy, Grade II or intermediate-grade malignancy, and Grade III or high-grade malignancy (anaplastic).

In Grade I there were 21 cases, 14 serous and 7 pseudo-mucinous. Eleven patients are living from 5 to 24 years after operation, but only 10 of these are free from disease. Seven who survived for 5 years had serous tumours, of which 3 were completely operable. All but 1 received X-ray therapy. The 4 others who survived for 5 years had unilateral completely operable pseudo-mucinous tumours, and 2 received X-ray therapy. In Grade II there were 23 cases, 19 serous and 4 pseudo-mucinous. Four patients are living; 3 are free from disease from 5 to 20 years after operation and 1 had a recurrence in the cervix after 7 years. Three of the 4 survivors had bilateral serous tumours. In 1 the growth was removed entirely but in 2 removal was incomplete. The fourth survivor had a completely operable unilateral pseudo-mucinous adenocarcinoma. All 4 received deep X-ray therapy. In Grade III there were 40 cases, 39 serous and 1 pseudo-mucinous. One patient is free from disease 21 years after complete removal of a unilateral serous papillary tumour (partly solid and partly cystic) followed by deep X-ray therapy. Two have been free from disease for less than 5 years. A 5-year study is possible in 68 patients. The total 5-year salvage rate is 20.5 per cent. The 5-year survival rate in Grade I was 62.5 per cent, in Grade II 15.8 per cent, and in Grade III 3 per cent. These figures emphasize the importance of grading in the prognosis of ovarian cancer.

The most important factor influencing prognosis is the extent of the growth. In 19 (22.6 per cent) the growth was completely operable, and 10 of these are free from evidence of disease from 4 to 24 years after operation; in 30 (35.7 per cent) it was incompletely operable, and only 4 were free from gross disease for more than 5 years; in 35 (41.6 per cent) it was inoperable, but 1 of these patients is alive with extensive disease still present 12 years after exploratory laparotomy.

The results substantiate the view that pseudo-mucinous tumours are less malignant than the serous variety. Of the 68 patients who had serous growths and have been followed up for over 5 years 9 are free from disease, while of the 10 with pseudo-mucinous tumours 5 are alive and well. At least three pathological entities are of prognostic importance, that is, the papillary cysts, the partly solid and partly cystic tumours, and the solid tumours. Twelve of the 16 patients alive for 5 or more years had papillary cysts. Only 4 of the 37 with partly solid and partly cystic tumours have survived more than 5 years, and all of the 18 who had solid cancers are dead.

Of 10 patients with granulosa-cell tumours 4 are alive and free from recurrence but only 3 for more than 5 years; 3 are dead. One of these died of cerebrospinal syphilis, another from X-ray damage to the large bowel, and the third died 8 years after incomplete operation. There were 7 cases of ovarian carcinoma associated with adeno-carcinoma of the endometrium. One patient is alive and well 1½ years after operation. Two patients with dysgerminomata have remained well for 3 and 24 years; 2 with adenocarcinomata developing in teratomata are dead. One patient who had a Brenner tumour is well 8 years after operation and 1 with a Krukenberg tumour died 3 months after operation.

The authors conclude that operability and grade of malignancy are undoubtedly the factors that influence prognosis. Although many ovarian

tumours are silent or nearly so, 37 per cent of the author's patients had abdominal symptoms, mostly referable to the gastro-intestinal tract, for 6 months to several years before a pelvic examination was made. Doubt is cast on the value of peritoneoscopy in diagnosis, for the ovary is often difficult to visualize if it is not enlarged, especially in obese women. If malignant disease of the ovary is to be detected at an early stage in more than an occasional patient, routine 6-monthly pelvic examinations will have to be carried out.

F. J. Browne

1994. **Thecoma of the Ovary and Carcinoma of the Endometrium.** (Tecoma del ovario y carcinoma del endometrio.)

By J. C. AHUMADA, R. SAMMARTINO, and J. L. SARDI. *Obstet. Ginec. lat.-amer.*, **6**, 34–43, Jan.–Feb. 1948. 5 figs., 12 refs.

The association of an ovarian thecoma (xanthofibroma theco-cellularis of Loeffler and Priesel) with carcinoma of the endometrium has been noted by several workers. This coincidence has led to the hypothesis that the malignant tumour of the uterus results from the prolonged stimulation of the endometrium by oestrogenic hormone produced in the ovarian tumour. The authors describe 3 cases. In the first case a diffuse carcinoma of the endometrium was found in association with incipient thecomata in both ovaries. In the second case, there were irregular areas of atypical endometrial proliferation. In some of these areas cystic glandular hyperplasia was present with neoplastic proliferation in other areas. The left ovary contained a thecoma measuring 10 × 8 mm. In the third case the endometrium at the fundus uteri was polypoidal. Elsewhere in the uterus it was atrophic. Several intramural fibroids were found. In the polypoidal endometrium there were glandular proliferation, with many atypical nuclei and areas of stratification typical of adenoacanthoma, and a right hydrosalpinx. The left ovary contained a small multicentric thecoma.

The authors conclude that the co-existence of hyperplasia of the endometrium with thecoma of the ovary is relatively common. In these cases it is impossible to decide whether there is a carcinoma of the endometrium or a carcinoid hyperplasia of the endometrium. It seems, in fact, that these conditions of the endometrium are caused by thecomata in the ovaries. In all cases the atypical proliferation of the endometrium is preceded by hyperplasia of non-specific origin. The ovarian thecoma must be considered as an important factor in the production of post-menopausal hyperplasia of the endometrium. In many cases the tumour in the ovary is so small that it is overlooked at gynaecological examination. In every case of post-menopausal hyperplasia of the endometrium the existence of functioning ovarian tumour, thecoma, or granulosa-cell tumour, must be borne in mind.

[Since the original description of the thecoma in 1932, the number of cases recorded has increased almost annually. This is an important ovarian tumour and one which, as the authors rightly state, is often overlooked. This serves to emphasize the importance of careful treatment of cases of hyperplasia of the endometrium, not only after, but also at the time of the menopause. There is no doubt that in the majority of these cases hysterectomy is the safest treatment; whenever possible the ovaries should be carefully examined.]

Josephine Barnes

1995. **Pathology and Clinical Features of Fibroma Thecocellulare Xanthomatodes of the Ovary.** (Zur Pathologie und Klinik des Fibroma thecocellulare xanthomatodes ovarii.)

By K. JAROSCHKA. *Zbl. Gynäk.*, **69**, 1228–1232, 1947. 3 figs., 8 refs.

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By W. C. REINER. *West. J. Surg. Obstet. Gynec.*, **56**, 205–207, Apr. 1948. 4 figs., 4 refs.

1997. **So-called Brenner Tumours.** (Ueber sogenannte Brenner-Tumoren.)

By O. PENDL. *Wien. klin. Wschr.*, **60**, 414–418, July 2, 1948. 52 refs.

1998. **Papillary Cystadenocarcinoma of Both Ovaries. Report of a Case with Apparent Cure Eight Years After Operation.**

By G. L. GAUDRAULT. *New Engl. J. Med.*, **239**, 56–57, July 8, 1948. 1 fig., 4 refs.

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By R. GANSE. *Zbl. Gynäk.*, **69**, 1205–1206, 1947.

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By P. B. RIBEIRO. *Rev. brasil. Cir.*, **17**, 327–332, June 1948. 3 figs.

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By J. H. ZEIGERMAN. *Amer. J. Obstet. Gynec.*, **56**, 187–190, July 1948. 3 figs., 4 refs.

2002. **Contributions to the Study of Metastic Tumours of the Ovary. Krukenberg's Tumour.** (Contributo allo studio dei tumori metastatici dell' ovaio tumori di Krukenberg.)

By F. TRUINI. *Clin. nuova*, **6**, 63–71, 1948. 4 figs., 13 refs.

2003. **Meig's Syndrome. Report of a Case of Fibroma of the Ovary with Ascites.**

By W. L. SIBLEY. *Sth. Surg.*, **14**, 456–461, July 1948. 2 figs., 26 refs.

2004. **Ovarian Fibroma with Ascites and Hydrothorax. (Meig's Syndrome.)** [In English.]
By N. CLEMENTSEN. *Acta obstet. gynec. scand.*, **28**, 96–104, 1948. 21 refs.

2005. **Fibroma of the Ovary with Ascites and Hydrothorax.**
By P. M. SPURNEY. *Ohio St. med. J.*, **44**, 722, July 1948. 11 refs.

2006. **Two Cases of Granulosa-cell Tumour.** (Sôbre dois casos de tumores de células granulosas.)
By W. PAIXAO. *Rev. Ginec. Obstet.*, **1**, 295–308, May 1948. 2 figs., 21 refs.

2007. **Ovarian Teratoma with Rupture into the Bladder, Ileum and Rectum.** (Teratom des Ovariums mit Durchbruch in die Harnblase und Ileum bzw. Rektum.)
By W. BROSIG. *Zbl. Chir.*, **72**, 1319–1326, 1947. 5 figs., 31 refs.

2008. **Primary Teratomatous Chorionepithelioma of the Ovary. Report of a Case.**
By H. M. OLIVER and E. O. HORNE. *New Engl. J. Med.*, **239**, 14–16, July 1, 1948. 2 figs., 28 refs.

2009. **Ovarian Dysgerminoma.**
By A. F. PAGANO. *Amer. J. Obstet. Gynec.*, **55**, 1058–1059, June 1948. 2 figs.

2010. **Endometriosis.**
By J. V. MEIGS. *Ann. Surg.*, **127**, 795–809, May 1948. 29 refs.

2011. **The Part Played by Endometriosis in Gynaecological Conditions.** (La place de l'endométriose en gynécologie.)
By P. BROCQ. *Rev. brasil. Cir.*, **17**, 289–296, June 1948.

2012. **The Use of Multiple Sources of Radium within the Uterus in the Treatment of Endometrial Cancer.**
By A. N. ARNESON, W. W. STANBRO, and J. F. NOLAN. *Amer. J. Obstet. Gynec.*, **55**, 64–78, Jan. 1948. 16 refs.

More contributions are appearing on the subject of the scope of modifications of Heyman's method of treating cancer of the uterine body by irradiation. In the present paper the authors examine their results in 93 cases treated between 1936 and 1941 inclusive. Hysterectomy was performed in 18 cases with a 5-year survival rate of 84 per cent; 32 cases were treated by irradiation followed by hysterectomy, with a 5-year survival rate of 18 per cent; 43 cases were treated by irradiation alone, and the 5-year survival rate was 27 per cent. [Careful examination of these figures is necessary to see which patients were operated upon and which had irradiation; also, the methods of irradiation changed in the period under review.] Until 1938 a tandem applicator was used; since then the technique has been altered to one in which multiple capsules are packed into the cavity. Before application of the radium a course of deep X-ray therapy is given (four pelvic fields and a total dose to each area of about 1,200 to 1,600 r). The survival rate for 5 years in the whole series was 53 per cent. The best prognostic sign was found to be the disappearance of the tumour in the uterus after pre-operative irradiation. The survival rate also varied with the uterine size and the histological type of the growth.
Kenneth Bowes

2013. **Leiomyofibroma of the Fallopian Tube.**
By S. W. STRINGER. *N. Y. St. J. Med.*, **48**, 1621, July 15, 1948. 1 fig., 15 refs.

Operations.

2014. **Necrotizing Enteritis as a Postoperative Complication in Gynaecology.** (Der Darmbrand als postoperative Komplikation in der Gynäkologie.)
By H. E. RUTHER. *Geburtsh. u. Frauenheilk.*, **8**, 467–478, June, 1948. 1 fig., 19 refs.

2015. **Vaginal Operation Technique.** (Zur vaginalen Operationstechnik.)
By F. FRIEDL. *Zbl. Gynäk.*, **69**, 1184–1188, 1947. 2 figs., 3 refs.

A description is given, with two photographs, of four new instruments for vaginal surgery. The first is a self-retaining speculum, the second an apparatus for suspending the legs in the lithotomy position, while the third and fourth are instruments for assisting the excision of the parametrium during radical hysterectomy. *S. S. B. Gilder*

2016. **A Multiple Sulfonamide Therapeutic Measure in the Postoperative Care of the Cervix and Vagina.**
By A. H. MARBACH. *Amer. J. Obstet. Gynec.*, **55**, 511–517, Mar. 1948. 24 refs.

After vaginal operations healing tends to be delayed because of the changes in the vaginal flora, the approach of the pH to neutrality, and the decrease of available glycogen. The author, in order to combat sepsis and promote healing, has introduced a cream containing 3.42 per cent sulphathiazole, 2.86 per cent acetyl-sulphanilamide, 3.7 per cent benzoyl-sulphanilamide, and 1 per cent urea peroxide. After tests to determine the toxicity and bacteriostatic power of the preparation it was used clinically in 200 cases—121 cases of conization of the cervix and 79 vaginal plastic operations. Within 24 hours after operation approximately 5.0 g. of the cream was inserted into the vagina twice daily. Malodorous discharge was non-existent in all the treated cases and healing time of the mucosal surfaces was reduced to 50 per cent of that in control cases. *F. J. Browne*

2017. **A Simple Instrument for Puncture of the Pouch of Douglas.** (Egyszerü esköz a Douglas tasak és méhfüggélekek kémlö szúrásához.)
By E. BURG. *Orv. Lapja*, **4**, 561–562, Apr. 25, 1948. 2 figs., 5 refs.

2018. **Fistula of the Upper Part of the Sigmoid due to Operative Trauma. Intervention through the Posterior Fornix, and Cure.** (Fistola della porzione alta del sigma da ferita operatoria. Intervento attraverso il fornice posteriore e guarigione.)

By A. FORNERO. *Monit. ostet.-gynec.*, **19**, 87–91, Mar.–Apr. 1948. 2 figs.

2019. **Analgesia of the Hypogastric Ganglion in Diagnostic Curettage.** (L'anestesia del ganglio ipogastrico nel raschiamento diagnostico.)

By G. DE GIOSUE. *Monit. ostet.-ginec.*, **19**, 5–12, Jan.–Feb. 1948. 13 refs.

The author has performed infiltration of the hypogastric ganglion, using the method of Gellert, on 50 women who were afterwards subjected to diagnostic curettage. In nearly all these cases, particularly when infiltration was preceded by administration of morphine, the results were very satisfactory and dilatation and curettage were carried out without causing pain.

Gellert's technique (*Zbl. Gynäk.*, 1926, **14**, 117) is simple. It includes disinfection of external genitalia and the vagina, exposure of the uterine portio with a speculum, application of a volsellum forceps to the cervix, and exertion of traction in a direction opposite to the side on which the needle is to be introduced. The needle should have a calibre of 1.5 mm. and a length of 10 to 12 cm. It is introduced into the lateral fornix to a depth of about 2 cm., with a slightly posterior inclination. Ten to 15 ml. of the analgesic solution is slowly injected, after aspiration has shown that no blood vessel has been entered. The fluid is introduced without force. The procedure is repeated on the opposite side. After 10 minutes the operation is begun.

The author, who studied 50 cases at the Obstetrical and Gynaecological Clinic of the University of Florence, found dilatation of the cervical canal very easy to perform in his patients and ascribes this fact to loss of tone of the circular muscle fibres. No untoward effects of blocking the hypogastric ganglions were noticed, apart from slight signs of shock in exsanguinated patients. The postoperative course was uneventful and afebrile in all cases. In 5 cases analgesia was not produced. In 3 of these the uterus was retroverted and the failure is ascribed to this. *Nicholas Alders*

2020. **Changing Concepts in Cervical Biopsy.**

By K. E. COX, V. B. BUHLER, and W. C. MIXSON. *Amer. J. Obstet. Gynec.*, **56**, 112–122, July 1948. 7 figs., 4 refs.

2021. **Uterine Suspension: A Report of Results.**

By W. H. VOGT, R. V. BOEDEKER, and G. LOPEZ. *Amer. J. Obstet. Gynec.*, **55**, 1044–1047, June 1948. 1 ref.

2022. **The Frequency of Hysterectomy for Benign Uterine Disease.**

By H. D. LAFFERTY. *Pennsylvania med. J.*, **51**, 993–997, June 1948. 2 figs., 12 refs.

2023. **Prolapse of the Vaginal Vault Following Hysterectomy. A New Method of Repair.**

By H. N. SHAW. *West. J. Surg. Obstet. Gynec.*, **56**, 127–133, Mar. 1948. 7 figs., 3 refs.

Three cases of prolapse of the vaginal vault after hysterectomy are described. The prolapse was repaired from above by using two vertical strips of anterior rectus sheath, hinged below and each passed medial to the corresponding rectus muscle and extraperitoneally to be attached to the cervical stump or vaginal vault. The operations were all performed less than 6 months before the cases were reported, and the results are not discussed.

Aileen M. Dickins

2024. **The Present Status of Female Sterilization Techniques in the United States.**

By R. J. MCNEIL and A. N. WEBB. *Calif. Med.*, **69**, 39–46, July 1948. 5 figs., 13 refs.

2025. **Injuries to the Bladder in Gynaecological Surgery.**

By J. K. FEENEY. *Irish J. med. Sci.*, **6**, 112–120, Mar. 1948. 6 refs.

The bladder is most likely to be injured in total hysterectomy, Wertheim's hysterectomy, and plastic operations for vaginal prolapse. The bladder may be injured in abdominal operations: (*a*) During incision of the parietal peritoneum. This accident can be avoided by continuous drainage of the bladder for the half-hour immediately before operation, by making the peritoneal incision in the upper limits of abdominal wound, and by suspecting the presence of a high bladder when the tissue on separation of the recti muscles has a fleshy appearance, and incision into it causes venous oozing. (*b*) In the downward displacement of the bladder before the uterine arteries are clamped and the vagina opened in total hysterectomy. Failure to displace the bladder well downwards may result in injuries during division of the anterior vaginal wall, during clamping of the lateral cervical attachments, and during suture of the vaginal angles. Over-vigorous displacement of the bladder may damage the muscle wall or its blood supply and give rise to a vesico-vaginal fistula at a later date. (*c*) During operation for cervical and broad ligament fibroids, in operations for pyosalpinx, and in Millin's extraperitoneal fascial strap operation for stress incontinence of urine. The bladder and ureters should be dealt with under direct vision in a Wertheim hysterectomy.

In the author's series of 270 abdominal hysterectomies the bladder was injured in 4 cases. He has also treated 5 cases operated on by other surgeons. These 9 cases are reviewed in detail. The bladder may be injured in vaginal operations, if care is

not exercised in dividing the vesico-cervical ligament and the pillars of the bladder. Postoperative necrosis and fistula formation may result from over-vigorous digital pressure or blunt dissection during upward displacement of the bladder. The repair of a vesico-vaginal fistula after abdominal or vaginal hysterectomy may prove difficult. As such fistulae have a tendency to spontaneous cure, no attempt should be made to repair them until a minimum period of 3 months has elapsed. Urinary infection must be overcome by intensive treatment with ammonium chloride and sulphonamides. The operation should be deliberate and methodical, after the situation of the fistula has been clearly defined. As it is sometimes impossible, on account of the inaccessibility of the fistula and the formation of scar tissue, to utilize an accurate flap-splitting technique, the fistula should be dealt with by elliptical excision, the adherent margin being freed and united in 2 layers with interrupted catgut, 000 plain catgut for the bladder and 0 chromic for the vaginal mucosa. A self-retaining catheter is left in the bladder after operation for a period of 12 to 21 days. A free flow of urine through the catheter is maintained continuously by day and night. The reaction of the urine is tested four times daily and twice during the night, and kept acid by large doses of ammonium chloride. Sulphonilamide was found to be the most efficacious sulphonamide. *T. N. MacGregor*

2026. **Surgical Treatment of Rectal Complications of Radiotherapy of Carcinoma of the Cervix.** (Traitement chirurgical des complications rectales de la radiothérapie pour cancer du col utérin. Possibilités de la chirurgie sympathique.)

By M. DARGENT and L. EICHOLZ. *Lyon chir.*, **43**, 199–218, Mar.–Apr. 1948. 8 figs.

In spite of careful assessment of dosage and distribution in radiotherapy of cancer of the cervix uteri this treatment is sometimes followed by local complications, particularly in the rectum. There is often a simple rectal irritation, with diarrhoea, which occurs from the eighth to the fifteenth day after the radiotherapy and soon subsides under treatment by opiates and wash-outs. Of 408 cases treated in the last 5 years the authors found 25 patients with more serious lesions; 6 had a definite proctitis and 12 a reaction which caused a slight stricture, while 5 developed a more severe stricture; and there were 2 recto-vaginal fistulae. Several patients had associated lesions in the sigmoid or small intestine, and in some cases there was development of malignancy in the rectum or pelvic lymph nodes. The rectal lesions were sometimes due to faulty technique but, as in the case of a crateriform ulcer, occasionally were almost unavoidable.

Surgical treatment is directed towards relief of pain and correction of the obstruction due to the rectal narrowing. Left inguinal colostomy gives relief but is unpleasant. It was found that by lumbar sympathectomy both symptoms were relieved and colostomy was usually avoided. In cases of pronounced obstruction temporary colostomy enabled the strictured part of the rectum to be excised, after which the opening in the sigmoid was closed. Sometimes relief was obtained merely by injecting the lumbar sympathetic with a local analgesic; this method was suitable for the early and ulcerative form of reaction affecting the anterior wall of the rectum. *Zachary Cope*

Miscellaneous.

2027. **A Rare Case of Idiopathic Inversion of the Uterus.** (Idiopathias méhkifordulas ritka esete.)

By S. ARVARY. *Orv. Lapja*, **4**, 562–564, Apr. 25, 1948. 1 fig.

2028. **Mucous Membrane Changes of the Vulva in Pernicious Anaemia.** (Möllersche Schleimhautveränderungen an der Vulva.)

By A. KATHE. *Derm. Wschr., Leipzig*, **119**, 148–156, 1947. 3 figs., 7 refs.

The changes of the vulva which the author describes are similar in character to glossitis in pernicious anaemia. The lesions consisted of bright red patches of erythema, often symmetrically arranged. In several patients they gave rise to a burning sensation. Like the glossitis, the condition was often found to precede frank pernicious anaemia by many years. More rarely the same condition accompanied hypochromic anaemia. These vulval changes responded to liver and iron therapy respectively. The differential diagnosis is discussed and particular mention is made of trichomonas vaginitis, tertiary syphilis, and lichen planus. Three fully developed and 5 suspected early cases of pernicious anaemia with these vulval changes are presented. As these changes are often precursors of pernicious anaemia, their discovery should lead to early diagnosis and specific treatment.

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